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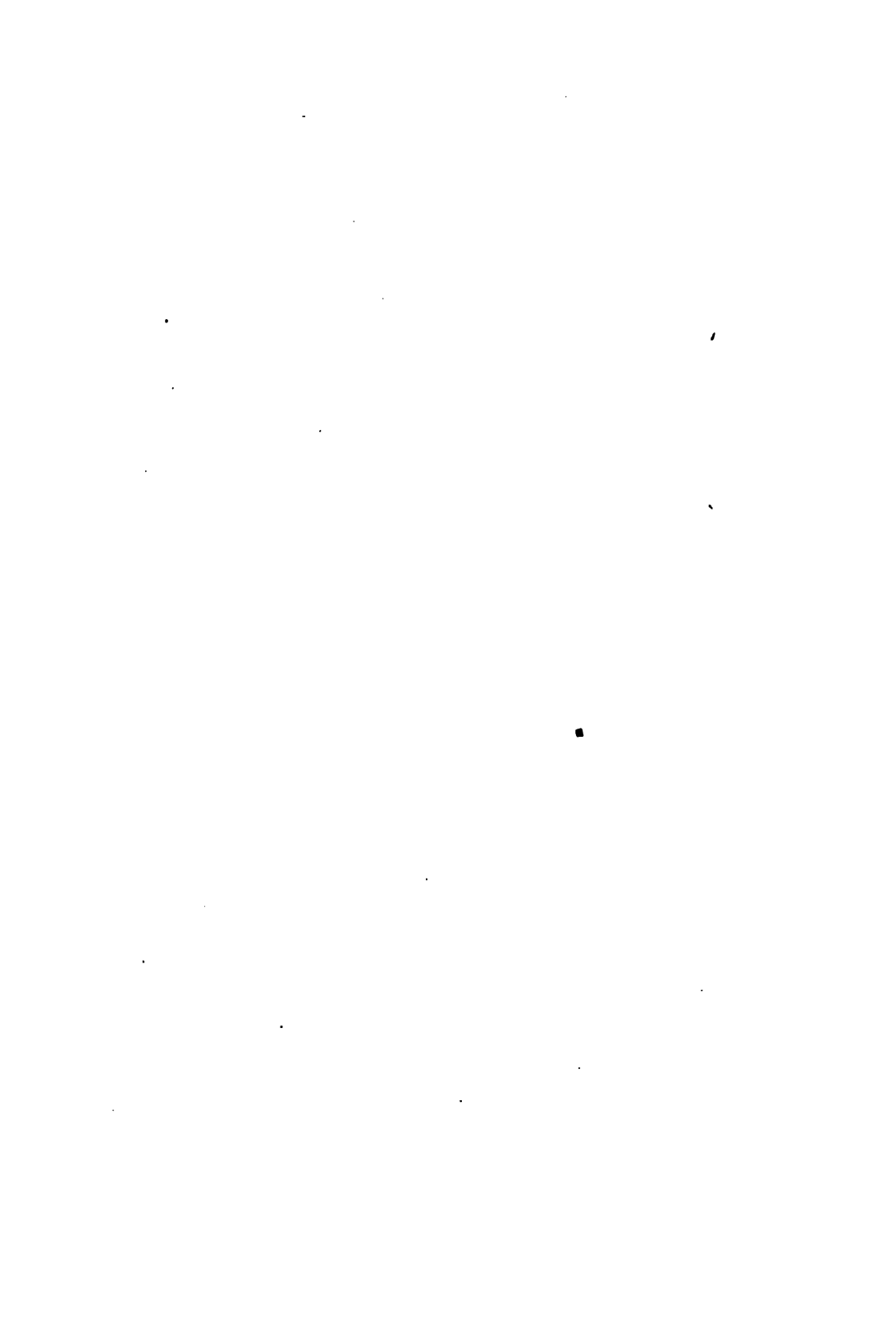
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GENERAL PATHOLOGY

AND

PRINCIPLES OF MEDICINE

FOR

STUDENTS AND PRACTITIONERS OF DENTISTRY

BY

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ILLUSTRATED WITH 118 ENGRAVINGS AND
6 COLORED PLATES



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PREFACE.

THE justification of this manual is the need of a text on general pathology suitable for dental students. It is based on the course given in the Dental College of Western Reserve University. A number of years of experience as a teacher of this subject has led to the conviction that a great deal of applied pathology and some clinical medicine are best included in this course. There is a tendency of late to correlate these two aspects of medical science more closely in the complete texts in pathology for medical students. For the dental students it is especially important and necessary that the subject be considered in this way. So far the dental curriculum has provided very limited time for this subject, which represents the point of contact of dentistry with general medicine. Very little time is given to the principles of clinical medicine in any other course, except under the heading of oral surgery. Accordingly it is hoped that the consideration of many clinical and applied subjects on the basis of pathology will be judged as an adaptation to the needs of the present dental student. Special emphasis is put upon the oral manifestations of systemic disease. The last three chapters deal with the special pathology of the oral cavity and related structures and with the subject of focal infection.

V. C. R.

CLEVELAND, OHIO, 1921.

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DENTAL PATHOLOGY.

INTRODUCTION.

To the student of dentistry the application of general pathology to his chosen art cannot be fully apparent at the outset of his studies. By way of introduction a few facts may be considered to show how closely dentistry in its broadest aspects is related to medical science. As soon as one penetrates the enamel layer of a tooth he is dealing with living tissues, which are integral parts of the general bodily organism. The same blood constantly circulates through the roots and pulps of teeth that circulates through the heart, brain, joints, kidneys and the remotest parts of the body. Germs and their poisonous products liberated at the roots of teeth are carried into the general circulation and, conversely, poisons of disease anywhere in the body are poured into the blood stream, which supplies the living tissues of the teeth. The blood is a most complex chemical substance, receiving from the innumerable groups of cells which it bathes a great variety of products. The so-called internal secretions of the ductless glands are absorbed into the general blood stream to control development and nutrition in very distinct parts, including the teeth. The conformation of the jaw is determined by the secretions of the pituitary gland. Acromegaly is a disease characterized among other things by an overgrowth of the jaw due to disturbed pituitary secretion. The system of internal glands exerts a very nicely balanced regulatory influence on the body functions. These secretions are, of course, normal constituents of the blood. Obviously all the abnormal products of disease are brought similarly in contact with the living tissues, including the teeth.

From a still more practical standpoint, general pathology is necessary for an understanding of the oral manifestations of systemic disease. For example, syphilis, often in its most infectious forms, occurs as lesions in the mouth. The disease might very readily be inoculated into the dentist's finger by a puncture wound or through a minute skin defect, or it might be carried on an unsterilized instrument to another patient. A proper realization of the need for asepsis in dentistry cannot be gained except by a study of the principles of pathology and of the elements at least of clinical medicine. Unless the dentist knows that the causative agent of many infectious diseases, from colds to cerebrospinal meningitis, may be present in the oral secretions of his patient, his aseptic technic sooner or later is very apt to become most perfunctory in character. The administration of general anesthetics by dentists certainly makes some knowledge of elementary clinical medicine highly desirable. Grave heart disease may be suspected by blueness or cyanosis of the lips and gums and severe anemia by the pallor of the mucous membranes.

In short, dentistry is but a special field of medicine. The two were originally the same profession and of late years as the dental field enlarged to Oral Surgery, Orthodontia, and Prophylaxis of Oral and Systemic Infections, Dentistry and Medicine are again coming closer together.

CHAPTER I.

PATHOLOGY.

PATHOLOGY is the science of the anatomical and functional changes produced by disease. It is fundamental in the science of medicine and in all its subdivisions. It is due to the science of pathology that medicine emerged from superstition and the crudest empiricism of previous centuries. It is doubtful whether there can be a functional disorder without a corresponding physical change in the cells of the tissues. As the methods of examination become more refined, disturbances once supposedly functional have been found to be associated with structural changes. However, many organs with disordered function still fail to show anatomical changes appreciable by our present means of investigation. Consequently pathological physiology has come to be a recognized department of general pathology. For example, a perverted secretion of the salivary gland due to abnormal excitation of the secretory nerve fibers would lie in the field of pathological physiology. Similarly pathological chemistry is a department of general pathology in which very extensive research has been carried out of late years. Chemical processes in the tissues, however, are included in physiology in its broadest sense under the heading of metabolism. Accordingly there are three main divisions of general pathology:

1. **Etiology**—the science of the causation of disease.
2. **Morbid anatomy**—the study of the structural changes produced by disease.
3. **Pathological physiology** dealing with the effects produced by disease in the form of disturbed functions, which are really the clinical symptoms of disease.

Health of tissue then means an absence of harmful agents—normal structure and normal function. It implies a nice

balance between the constructive (anabolism) and destructive (katabolism) processes involved in the nutrition of tissues. The simplest example of this is the assimilation of oxygen carried in the hemoglobin of the blood by the cells of the tissues and the elimination of carbon dioxide. Either insufficient oxygen or an accumulation of carbon dioxide would constitute a minor departure from perfect health of tissues.

CHAPTER II.

ETIOLOGY—EXTRINSIC CAUSES OF DISEASE.

It is useful to classify all the causes of disease under general headings so that the various reactions of living tissues to injurious agents can be classified and studied. Causes of disease are sometimes divided into *predisposing* and *exciting* or determining—the former indicating factors that favor the development of disease, but do not directly cause it; such as bad air and insufficient food in tuberculosis: the latter being the necessary factor which directly starts the disease process—the bacillus of tuberculosis. Causes of disease are also classified as extrinsic and intrinsic, depending on whether the causative agent originates outside or inside the body. The extrinsic causes are included under the following headings:

1. **Trauma.**—Direct injury, mechanical or chemical. This is the simplest cause of structural abnormality in the tissues. Cutting, contusing or crushing causes, if severe, death of the cells (necrosis), if slight and repeated, various vital reactions occur in the tissues—most commonly inflammation but also other pathological processes. Trauma may also act as a predisposing cause of disease by lowering local resistance to infection or by stimulating the cells to the overgrowth of tumor formation. Practically the effect of trauma is seen in a great variety of ways. In orthodontia, excessive pressure brought to bear on the teeth and alveolar structures lowers resistance and leads to infection. This infection and inflammation may promptly subside if the trauma is removed, and the cells return to the healthy state, in which immune substances protect against infection.

2. **Fatigue.**—A definite departure from health of tissues occurs in fatigue by the accumulation of toxic chemical bodies in the form of waste products, which are eliminated

normally—that is when there is an adequate amount of rest. As stated before, the processes of destruction are in excess of the processes of construction and excretion. Sarcoplactic acid accumulates in the muscles and in the various organs, a variety of abnormal substances which cannot be identified chemically. Some recent experimental work has been done to determine the nature of the toxins of fatigue. No very highly toxic substances could be found, but it is important to grasp the conception that extreme fatigue is in the nature of a toxemia. The body is poisoned in mild degree and manifests the condition by clinical symptoms similar to those produced by true intoxications. The neuralgic pains of fatigue are only quantitatively different from the neuritis of poisons to be taken up later. Fatigue also acts as a predisposing cause of disease, especially by lowering resistance to infection. Tuberculosis or pneumonia more easily attacks the fatigued individual. Focal infections such as blind abscesses at the roots of teeth are enabled to break through the local defenses and spread to adjacent parts or into the blood stream. In this way infection may become generalized and destroy the patient. Consequently rest in bed is of the first importance in a patient with a spreading infection especially in an elderly person or one with chronic disease, draining his resistance. Local rest to an affected part is also of importance. It is common knowledge among surgeons that an infection of the hand is much more promptly controlled if the forearm is put on a splint than if the hand and fingers are freely moved. In a tooth infection spreading into the neck, rest in bed serves to immobilize the parts to a degree as well as to prevent general fatigue of the body. Rest is fundamental in the treatment of all infectious diseases. Prolonged fatigue leads to a condition of hypersensitiveness of the nervous system termed somewhat indefinitely neurasthenia. Neuralgic pains are experienced all over the body. Functions of organs are impaired. Hysterical outbursts occur and the patient generally is in “delicate” health. The important point practically in regard to these cases is to exclude any obscure disease before making the diagnosis of neurasthenia.

3. **Heat.**—The body in health maintains an approximately uniform temperature. The heat-regulating mechanism protects against variations in temperature in the environment. Heat effects may be:

A. *General.*—When the whole body is subjected to excessive heat, which finally overcomes the heat-regulating mechanism in one of two ways:



FIG. 1.—Generalized sweating from heat stroke.

(a) *Heat Stroke, or Thermal Fever*, in which there is excessive fever (hyperpyrexia) sometimes as high as 105° . This is usually due to direct exposure to the sun's rays and must be combated by withdrawing heat by cool baths.

(b) *Heat Exhaustion*, in which there is moderate temperature sometimes as low as 95° . The condition is more, akin to shock and is the more serious form of heat prostration. It is usually due to excessive temperature in enclosed spaces.

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It must be treated as other conditions of shock are treated, by external heat and stimulants.

B. *Local*.—Burns result from local heat. If the burn extends over considerable surface especially upon the abdo-



FIG. 2.—Cicatricial contraction from an old burn. Side view.

men, there is extreme or even fatal shock. Large burns also produce systemic disturbance and high fever from the absorption of toxic products of decomposition in the destroyed tissues. Subsequently in burns involving the true skin, there is marked contraction of cicatricial tissue, leading

to extreme deformities in severe cases. In bad burns of the neck, the lower jaw may be bound down and fixed to the clavicle by dense scar tissue. For practical purposes burns have been classified into four degrees:

1. *Hyperemia*.—Simple redness of the skin due to vasodilatation—the first effect of heat.

2. *Vesication*.—Blistering due to the extravasation of serum under the epidermis.



FIG. 3.—Microscopic tissue changes in the hyperemia and inflammation of a burn.

3. *Destruction of the True Skin*.—This is the first stage to leave permanent scars.

4. *Carbonization* or complete charring of the tissues.

Prolonged high temperatures lead to disturbances of metabolism, which produce abnormal chemical substances or poisons. In this way the vital resistance of the body is reduced as described before. Many evidences of tissue degeneration have been observed in connection with the effect of high temperatures. It will be seen that the various etiological agents operate similarly in a very general way—namely by disturbing the chemical normality of the tissue.

4. **Cold.**—The heat-regulating mechanism of the body is less effective in exposure to cold than to heat since it acts only by retaining the body heat. Any factor such as starvation which reduces the processes of oxidation in the body conspires with external cold in lowering the body temperature. The first reaction is increased muscle tone and clonic contractions, shivering, which produces heat. There is also mental stimulation. Later there is an irresistible desire to sleep. The nervous system generally is depressed. Respiration becomes shallow and muscles become stiff and weak. The body temperature may fall as low as 70° F. before death.

Head Colds.—Exposure to cold is a predisposing cause to a number of diseases, especially acute infections of the respiratory tract—hence the expression “catching cold.” Common colds, however, are infections of the nasopharynx. Their contagious character is generally recognized. Recent experimental work has shown that the infective virus of head colds can pass through a Berkefeld filter and produce a cold on being sprayed in the nasal cavities of animals and men. Benjamin Franklin observed long before the days of bacteriology that groups of men on hunting expeditions exposed to great hardships and low temperatures rarely developed colds, but when they returned to the city and mingled with people, they frequently took cold, the same as others. Cold and wet induce a congestion in the nasal mucosa almost at once. This may promptly subside but also strongly favors bacterial growth in the increased secretions. If the infection occurs, it runs a course quite similar to that of any other form of inflammation of mucous membrane. Cold also favors the extension of the infection along the mucous membranes and thus produces a pneumonia just as other predisposing causes favor extension of a focal infection. Pneumococci and influenza bacilli are most commonly found in respiratory diseases. Cold also acts as a predisposing factor in rheumatic fever especially following tonsillitis. Trifacial neuralgia may be precipitated by exposure to cold in a case with abscesses at the roots of teeth.

Frost Bite.—Locally the effect of cold is quite similar to that produced by heat. The primary effect of cold, however,

is to produce pallor due to vasoconstriction, which serves to prevent loss of body heat by radiation. The reaction to local injury by cold shows the following stages:

(a) *Hyperemia*.—Transient.

(b) *Vesication*.—The same as in burns.

(c) *Pallor*.—Occurring in exposure to very low temperatures as a result of extreme vasoconstriction.

(d) *Gangrene*.—In freezing, when the circulation has been stopped in a part and the tissues die.

Chilblain.—Repeated exposure to milder degrees of cold and especially when associated with moisture produces in susceptible individuals a peculiar vasomotor instability in the distal parts, usually the fingers and toes. Painful swellings of the affected parts with livid and purplish discoloration occur—commonly called chilblain. The condition persists a number of days after the exposure to cold and often leads to considerable desquamation. Later very mild degrees of cold and dampness are sufficient to produce recurrences.

5. Atmospheric Pressure Changes.—Minor variations in barometric pressure act as predisposing or contributory causes of disturbed functions. The susceptibility of certain patients with chronic diseases to weather conditions depends in part at least on changes in atmospheric pressure. Increased humidity lowers barometric pressure, since water vapor has a lower specific gravity than dry air.

Increased atmospheric pressure, or artificial air pressure, is used in caissons for tunnel construction and deep sea diving. The body tolerates high pressures quite well if compression and decompression are very gradual. Too rapid decompression produces quite serious symptoms commonly called caisson disease or “bends” since the victims are compelled to bend over with cramping pain in the abdomen and muscles. The symptoms are due to the release of bubbles of nitrogen in the blood stream and in the tissues. In addition to the abdominal cramps, there are pains in the joints and muscles sometimes with marked swelling, also vomiting, bleeding from mucous membranes, especially nose-bleed, delirium and due to lesions in the nervous system, a group of paralytic conditions, most commonly paraplegia

(paralysis from a certain level of the spinal cord down and involving both legs). The condition may be fatal but there may be recovery after prolonged shock and extreme subnormal temperature. The treatment is prompt recompression at the onset of symptoms and very gradual decompression.

Decreased atmospheric pressure on the body occurs in high altitudes and its effects are of importance in aviation. The symptoms are drowsiness, faintness, nausea, and hemorrhages especially nosebleed. It is said that an aviator is not safe at a greater altitude than 18,000 feet without an oxygen mask. The partial pressure of oxygen is of course low, but the body compensates quite satisfactorily by increased rate of respiration and heart beat and by an increased number of red corpuscles in the blood so that the respiratory exchange (absorption of oxygen and exhalation of carbon dioxide) is practically normal. Consequently the symptoms must be due in part at least to mechanical factors directly related to the reduced air pressure.

6. **Electricity.**—*Artificial currents* of the various kinds produce quite different effects on living tissues. The direct current stimulates or shocks only at "make and break" of the circuit. A uniform direct current of low ampèreage through a nerve muscle preparation produces no effect. A very small current is sufficient to stimulate and irritate a sensitive nerve. For example the miniature electric cell that is formed between two different kinds of metals in fillings separated by tooth substance causes pain. Direct currents of sufficient ampèreage burn the tissues, because of the high electric resistance of the latter. These burns are peculiar in several respects. They are very slow to heal. They are more severe at the points where the current enters and leaves the body. Extensive sloughing of the adjacent parts is frequent. Radiating tears are sometimes seen in the tissues. Fatal shock may result from a direct current of 500 volts in man. Some animals are much more sensitive, notably horses.

Alternating currents produce continuous shock and are the more dangerous. If the alternation is of extreme frequency as in the Tesla currents with high voltage and low ampèreage

the shocking effect is lost. However, industrial alternating currents and the faradic induced currents produce severe shock. The reaction of muscles and nerves to faradic stimulation is lost in certain organic diseases of the nervous system such as infantile paralysis. This "reaction of degeneration" is accordingly used as a test. Electricity is used rather extensively in therapeutics, but it has no known specific effect in restoring health to tissues. It has some value as a stimulant in exercising weakened or parietic muscles. For this the direct or galvanic current is said to be more efficient.

Lightning is a discharge of static electricity of high voltage producing shock like that of artificial currents except that there is extreme disorganization of tissues. Sometimes there occur arborescent tracings representing the course of blood-vessels. Lightning like other forms of static electricity discharges to sharp points and vertical objects in an open field such as an isolated tree or a lightning rod on a building. Secondary currents are induced in metal objects near a "stroke" of lightning, so that slighter shocks may be received. Many of the non-fatal shocks are of this character. Prolonged measures of resuscitation should be carried out in all cases—artificial respiration, external heat and stimulants.

7. X-ray, Radium and Other Forms of Radiant Energy.—By many unfortunate experiences these agents were found to have very profound effects on cellular processes. The physics of radiant energy is of course still in the experimental stage, but additions to the knowledge of the subject are made each year. One simple conception, which in a general way is true, is as follows: Radiant energy consists in transverse vibrations of the ether of the same velocity but of different wave lengths. Analyzed into a complete spectrum, the rays of greatest wave length are electric such as the Hertzian waves (of wireless telegraphy) which have no known influence on living cells; then in decreasing order of wave lengths, thermic rays of radiant heat; then infra-red light rays; then the optically visible light spectrum; then ultraviolet rays, which have a more marked effect in producing sunburn than ordinary mixed sunlight; and finally chemically active rays,

including *x*-rays and the still more penetrating gamma rays of radium. If this conception is true, the physical nature of the above phenomena is no more mysterious than that of ordinary light. The eye is capable of perceiving only a limited range of wave length, just as the ear perceives only certain wave lengths in the air vibrations of sound. The sun's rays contain a great variety of waves in varying concentration, so that sunlight is a considerable factor in biological processes. The shorter the wave length, the more penetrating and the more severe the effect.

Radium.—The emanations of radio-active substances such as radium, consist of so-called corpuscular rays, which are not primarily vibrations of ether, but streams of electrons thrown off with a velocity somewhat less than that of light. When these electrons impinge upon certain substances such as metal or glass, the ordinary ether vibrations are set up. This also occurs in the *x*-ray tube. The positively charged electrons or anode rays correspond to the Beta rays of radium and when they impinge upon the anode in the vacuum tube they produce *x*-rays. Beta rays from radium playing on metal or glass also set up short ether vibrations, the gamma rays, which are very closely related to *x*-rays. Practically the corpuscular rays and ether vibrations produce the same type of reaction on cells. Screens of various kinds of metals serve as filters of the various waves, so that the effects of each may be observed.

The ultraviolet rays have a strong irritant effect on the skin. Sunburn is largely due to them. Sunburn occurs more readily on mountain tops than at sea-level because the atmosphere absorbs these vibrations of the ether. The skin is injured by the rays and after a period of hours, an inflammatory reaction comes on, with dilatation of bloodvessels, transudation of serum and cellular changes characteristic of inflammation. Prolonged exposure to sunlight leads to a deposition of pigment or tanning, which is really a protective adaptation to environment. Hardening of the surface cells of the epidermis or keratinization also results in certain individuals, a process which is closely related to the cancerous overgrowth induced by the stronger, that is shorter, wave of *x*-ray. Certain

forms of artificial light as that of the electric arc have a larger proportion of ultraviolet rays than sunlight. In a general way the effect of light as applicable therapeutically is a mild stimulation to cell activity and growth.

X-rays produce a similar irritant effect on the skin and also to a less extent on deeper tissues. Screens can be used to protect the skin and allow the more penetrating rays to act on deeper organs. The reaction to *x-ray* or radium comes on only after about two weeks. It produces no sensation at the time of exposure although ordinary heat from the *x-ray* tube may be perceived. The reaction consists of redness, swelling, tenderness and all the signs of inflammation and later pigmentation and falling out of hair. If the exposure is severe and prolonged or repeated, the tissues are destroyed and sloughing ulcers result, which are peculiarly sluggish, and remain as open sores for months or years. The tissues adjacent to the ulcerated surface are also injured often with occluded bloodvessels, so that processes of healing are much impaired. Pathological tissues are more vulnerable than normal tissues and are consequently more readily broken down by the *x-ray*. Skin cancers can often be radically cured. The danger is always that some cells have extended deeper into the tissues or to the regional lymph glands beyond the effectual range of the *x-ray*. An overgrowth of scar tissue, such as a keloid, may sometimes be entirely absorbed under the influence of the *x-ray*. Repeated milder exposures produce a variety of degenerative changes. The hands of the radiologist before protective screens were used showed thin cracked skin, brittle nails, atrophied sweat glands and often skin cancers. Epithelial growth is stimulated. Microscopically, mitotic figures may be seen and epidermal buds growing into the corium. From this condition true epithelioma develops. The *x-rays* then may both produce and destroy cancer. The blood-forming organs are profoundly influenced by radiant energy. The main change is a loss of lymphocytes. The spleen and lymph glands are reduced in size and cleared of leukocytes. This effect is made use of in the treatment of leukemia. The genital glands in both sexes are also highly sensitive to the action of

the x -ray. Sterility in the male and artificial menopause in the female are quite readily induced with corresponding atrophic changes in the testes and ovaries. All other organs to a varying degree are affected similarly. X -rays have little if any effect on bacteria, while the alpha and beta rays of radium kill bacteria quite promptly. The knowledge of the different kinds of radiant energy is in its infancy. It is impossible to predict what the discoveries in the realm of physics may bring forth or what their application to biological problems may be. It is a growing field, in which truth must be slowly gleaned from many fallacious fancies.

CHAPTER III.

INTRINSIC CAUSES OF DISEASE AND INTOXICATIONS.

By contrast to the foregoing extrinsic causes of disease, the intrinsic causes should be separately considered, but as a matter of fact most intrinsic causes are associated at least indirectly with an extrinsic one. The bacterial diseases produce their pathological processes by the growth of bacteria within the body and the bacterial poisons, which are the direct cause of the symptoms of the disease, are formed within the body, but the original bacterium is introduced from the outside at some time. Even the intestinal tract is sterile at birth. Certain deficiencies or perversions of the glands of internal secretion of obscure origin may be taken as intrinsic causes of disease.

POISONS.

Since all these combined intrinsic and extrinsic agents really produce their effects by intoxications of some kind, the study of etiology will be continued by a classification of poisons. A *poison* may be broadly defined as any substance, which by contact with living tissues disturbs their structure or function. This of course includes the greatest variety of chemical substances from the toxic elements of mineral origin such as lead, arsenic and mercury to the complex toxins produced by living organisms, either vegetable or animal forms. Of vegetable origin also are the strong alkaloids—nitrogenous bases with powerful effects on living cells, especially of the nervous system. Cocain, morphin, and strychnin are among these. There are similar powerful poisons of animal origin such as ptomaines and venom of reptiles and insects.

The *fate of poisons* in the body is of considerable importance and practical value in treatment. There are three main ways by which the body if not overwhelmed by a fatal dose is relieved of poisons:

1. Elimination—through the various channels of excretion. Poisons may be discharged unchanged from the bowels, kidneys, lungs, skin, and in any of the glandular secretions, such as the saliva and tears and even the milk of a nursing mother, so that the welfare of the infant must be considered in case of poisoning and disease of the mother. Poisons show a selective action for certain organs or groups of cells both with respect to their injurious action and their channel of excretion. Accordingly elimination of poisons may be hastened by stimulating excretion through the various bodily emunctories. For example purges would be depended upon mainly if the bowel were the best channel of excretion and hot packs if the skin and sweat-glands were the most suitable outlet for poisons as is the case in Bright's disease.

2. Oxidation or other chemical alteration of the poisonous substances. Certain amounts of alkaloids and alcohol are completely oxidized. Carbolic acid is converted into an innocuous substance which is excreted through the urine.

3. Neutralization—by antibodies combining with toxins as a result of a vital protective reaction on the part of the body. This occurs mainly in connection with the infectious diseases such as diphtheria. Some toxins are neutralized by combining in a fixed chemical union with the cells of the body.

A simple classification of poisons is as follows:

- I. Exogenous—those poisons produced outside the body.
 - (a) Inorganic.
 - (b) Organic.
- II. Endogenous—those poisons produced within the body.
 - (a) Bacterial.
 - (b) Metabolic.

Exogenous Inorganic Poisons.—The exogenous inorganic poisons comprise mainly the strong acids and alkalies, the toxic elements and their compounds.

Acids.—The strong acids directly destroy cells by decomposing the proteid molecule. *Sulphuric acid* (H_2SO_4) abstracts water from organic substances and finally carbonizes them, so that a black or gray burn is characteristic of it. *Nitric acid* (HNO_3) forms a peculiar yellow compound with the proteid of the tissues called Xanthoproteic acid which serves to identify it among the strong mineral acids. Nitric acid is a powerful oxidizing agent and is used to cauterize diseased tissue and small benign tumors such as warts. *Hydrochloric acid* (HCl) produces a whitish discoloration and a tendency to surface “membranes” of destroyed tissue.

Alkalies.—Strong alkalies, sodium and potassium hydroxide (KOH and NaOH) also directly destroy living cells, but have in addition a characteristic softening, dissolving and hence penetrating effect. For this reason burns by alkali are more destructive than burns by acid and the subsequent inflammation and cicatricial contraction are more severe. The commonest illustration of this is the accidental swallowing of lye especially by children. The cicatricial contraction here leads to stricture of the esophagus.

Elements.—The toxic elements especially the metals make up an important group of poisons, which produce quite similar effects in the body and serve to illustrate how poisons in general act on the various systems of organs and what an important rôle they play in practically all pathological processes. The metallic poisons are of especial interest to the dentist, because many of the most readily recognizable lesions are in the mouth. The educated dentist may have the first opportunity of recognizing a chronic intoxication and of saving his patient from permanent invalidism just as the oculist may be the first to recognize by eye manifestations, an insidious disease of the kidneys.

Lead Poisoning.—The sources of lead poisoning have been very varied. The wide use of the metal in the industries has led to numerous epidemics. At present storage battery works are the most prolific source of acute poisoning. Painters, plumbers, typesetters and others have learned fairly well the dangers of lead. Lead faucets especially to cider or vinegar containers may be the source of consid

quantities of the very soluble acetate of lead. In the vicinity of lead smelting plants very toxic vapors may be inhaled. Even cattle grazing in adjoining fields, where the fine lead deposit accumulates, may show acute poisoning. Lead poisoning has also occurred from lead-containing plates for false teeth. The alimentary tract, the skin and the lungs are the main channels of absorption. In the acute cases the gastro-intestinal tract shows the most direct effects. The unstriated muscle is stimulated to a degree of contraction hardly equalled in any other condition. As a result there is intense colicky pain referred mostly to the epigastrium but also all over the whole abdomen. Severe vomiting usually occurs and occasionally considerable fever, so that the condition might easily be mistaken for acute appendicitis, especially when the history of exposure to lead is not at hand. Cases of this sort at operation have shown the most extreme contraction of the intestine, even to a caliber the size of the little finger and at intervals constricting rings even smaller. There is also extreme anemia of the bowel due to vasoconstriction and occasionally subperitoneal hemorrhages. The condition of the intestine fully explains the agonizing lead colic and the absolute constipation.

Chronic lead poisoning affects nearly all the tissues of the body. The "lead line" in the mouth is a deposit of sulphide of lead at the gum margin. The sulphur of decomposing protein material combines with the lead in the tissues. Consequently uncleanly mouths show the line earlier. Carefully kept mouths may show no line at all with a chronic poisoning of moderate degree. The lead line is not continuous but a series of bluish-black dots definitely within the gum tissue. It must be distinguished from a black deposit under a detached gum edge. As in all chronic poisonings the nervous system is particularly vulnerable. The peripheral nerves are first affected causing a neuritis, manifested first by pain and finally by paralysis. Lead has a predilection for the upper extremity and especially for the musculospiral nerve, so that wrist-drop is the characteristic deformity. However, neuralgic pains which are the first stages of neuritis may be felt all over the body especially as intercostal

PLATE I



Deposits of Sulphide of Bismuth in the Gums, Lips and Tongue in a Fatal Case of Bismuth Poisoning. The Bismuth was Injected in a Sinus in the Knee. (Courtesy of Dr. John Phillips.)

PLATE II



A Portion of the Lower Bowel in the Same Case of Bismuth Poisoning, Showing the Black Deposit on the Mucous Membrane. (Courtesy of Dr. J. Phillips.)

neuralgia, sciatica, headache and backache. The central nervous system is also disturbed. Insanity, the so-called lead encephalopathy may finally result. Degenerative changes also occur in the circulatory system. Arteriosclerosis or hardening of the arteries has long been recognized in lead workers. The red blood cells are attacked, so that a considerable degree of anemia results and slight jaundice from changed blood pigment. The body metabolism is perverted especially the metabolism of uric acid just as in alcoholic poisoning. Both intoxications predispose strongly to gout.

Bismuth Poisoning.—The use of bismuth in x-ray work and in the form of paste for injection into sinuses has of late years resulted in a considerable number of cases of poisoning by this metal. The mucous membrane of the mouth shows very striking discoloration due to the black sulphide of bismuth (Plate I). This may first come to the notice of the dentist and indeed the source of the bismuth may be the jaw in which a sinus has been injected with bismuth paste. The toxicity of this substance is not generally known. Clinical cases have gone undiagnosed to a fatal issue. They have also been confused with lead poisoning. Relatively small quantities may be fatal if injected into the tissues or into a sinus which subsequently heals on the surface. Stomatitis and serious poisoning have resulted from the use of bismuth subnitrate as a dusting powder on granulating wounds. Irrespective of the part of the body in which the bismuth is absorbed, there may be stomatitis and even ulceration of the buccal mucosa. The teeth often become loosened and necrosed and the tongue swollen and ulcerated. There are also profuse salivation, foul breath and acute tenderness and swelling of the glands of the neck. The gastro-intestinal tract as one of the channels of elimination is affected with increasing severity from above downward. Mild catarrhal inflammation in the stomach causes anorexia and vomiting. A more severe ileocolitis with the mucous membrane completely blackened by a film of bismuth sulphide (Plate II) causes diarrhea with blood, mucus and pus in the stools. Red blood cells are even more rapidly destroyed than by lead resulting in the most extreme degree of anemia. As also in

lead poisoning the nervous system is profoundly disturbed even to the point of generalized convulsions. Trismus may occur, a symptom of special interest to the dentist. Finally an acute inflammation of the kidneys (nephritis) through which bismuth is also excreted occurs as in so many intoxications. If bismuth salts are used in injections, an outlet at least for slow escape should be provided and maintained till the bismuth is fully eliminated, else serious or fatal poisoning may result. The subnitrate of bismuth taken in large doses by mouth may produce nitrite poisoning, by the reducing effect of the organic material. This is characterized by methemoglobinemia and cyanosis.

Mercury Poisoning.—This is seen most frequently in the medicinal use of mercury in the treatment of syphilis. It is often necessary to crowd mercurial treatment to the limit of tolerance of the patient in order to control a syphilitic process. Acute mercurial poisoning is seen after the ingestion of the bichlorid which may be taken accidentally or with suicidal intent. Acute poisoning may also result from the use of bichloride solution in irrigating large surfaces or abscess cavities. As an industrial poison it is much less widespread than lead. Acute mercury poisoning causes severe epigastric pain and fortunately when bichloride is taken by mouth, quite prompt vomiting in most cases. The vomitus may contain shreds of mucous membrane having a cooked appearance due to the coagulating effect of the corrosive sublimate in contact with the albumin of the tissues. Considerable bleeding may occur from the detachment of mucous membrane. A little later a metallic taste in the mouth and salivation occur. Then follow most characteristically acute suppression of urine with the onset of acute nephritis and diarrhea from enteritis. In an overwhelming dose, there is early collapse with irregular pulse and death within a half hour. Less severe cases at onset may die weeks later from the kidney involvement. One bichlorid tablet of $7\frac{1}{2}$ grains, the size most commonly on the market may easily cause death if not vomited. In fact fatal cases have occurred from as small a dose as 2.7 grains. An appalling number of deaths from accidental bichlorid poisoning occur each year

in this country. A ready antidote may be had in egg white or milk (to form an albuminate of mercury), in addition to emptying the stomach.

The chronic poisoning, however, is of more importance to dentists, since the earliest manifestations are in the mouth. Also in mercurial medication, the gum irritation is most severe at the point of any carious tooth or inflamed third molar. In fact dentists frequently receive patients in the most active and infectious stage of syphilis for care of the teeth in order that the patient may tolerate adequate treatment. They may or may not inform the dentist of their condition. Mercury causes a catarrhal inflammation in the whole alimentary tract, most marked in the mouth as stated, but also severe in the lower intestine. In the mouth red swollen gums occur with tenderness of the teeth on biting. Later there is a suppurative gingivitis and loosening of the teeth. Still later as has happened in an overdose of mercury, the teeth fall out from necrosis of the jaw. There may be a chronic enlargement of the salivary glands and persistent salivation. Nausea, vomiting and diarrhea result from the same type of mucous membrane inflammation in the lower alimentary tract. The nutritional disturbance may be very profound. Mercury can also cause a neuritis as other metallic poisonings, but fortunately its effect on nervous tissues is not so early as that of lead, arsenic and other metals.

Arsenic Poisoning.—The local caustic effect of arsenic is of importance to the dentists. It causes direct death or necrosis of cells with which it comes in contact in concentrated form. If a portion of an arsenical preparation escapes from a tooth to the adjoining gum, the latter soon shows a purplish discoloration, which later changes to a yellowish slough. If more arsenic finds its way into adjacent parts, there may be necrosis of bone with sequestrum formation. The pericementum may be destroyed so that one or more teeth drop out. Even extensive destruction of the jaw has occurred. In such cases, enough arsenic may be absorbed to cause general poisoning. The latter in acute form occurs also in the taking of such arsenic-containing poisons as Paris green either by accident or with suicidal intent. Poisoning has

occurred also with large doses of arsenical antisyphilitic preparations, notably salvarsan. The symptoms are intense pain in the stomach and vomiting as in mercurial poisoning. In very large doses there is prompt collapse and death. A grain and a half of arsenic may be fatal. Less severe poisoning causes an early acute nephritis and painful diarrhea, followed by the picture of chronic poisoning. This is seen most frequently as a result of the medicinal use of arsenic, which also is sometimes crowded to the limit of tolerance. Arsenic in the dye of wall paper and colored goods may escape in volatile compounds and lead to chronic poisoning. The specific effect of arsenic on the tissues is a paralysis of capillaries. This permits of an extravasation of fluid and explains many of the pathological changes of arsenic poisoning. An early puffiness of the eyelids is very characteristic. There are other localized edemas. The paralysis of capillaries in the intestine causes the peculiar watery diarrhea with the so-called "rice water stools." Fatty degeneration occurs in the various organs. Arsenic also has a severe toxic effect on nervous tissues. Peripheral neuritis may come on very rapidly with extreme wasting of the muscles of the extremities, more often the lower, than in lead poisoning, but also the upper extremity. Oral manifestations of arsenic poisoning are less prominent, but there may also be a definite stomatitis with salivation and red bleeding gums. It is instructive to note the similarity of the symptoms of the various metallic poisonings and indeed of all intoxications in a general way. As stated before, intoxications in the broad sense are responsible for a large part of pathological processes and of clinical symptoms.

Arsenic has in addition to the above actions the peculiar property of causing at least as a predisposing factor two distinct pathological processes: pigmentation and epithelioma. The skin shows a dark pigment in some cases after long administration of arsenic, possibly because arsenic is excreted in part through the skin. There is also a localized thickening of the epidermis (keratosis), which occasionally is the site of a true skin cancer. It will be recalled that radiant energy in the form of x-ray may also cause epithe-

lioma. These facts will be of interest later in the study of the vexed problem of the etiology of cancer.

Phosphorus Poisoning.—As a final example of poisoning by the toxic elements, phosphorus may be considered because of the oral lesions and the value of dental prophylaxis. The acute poisoning, such as occurs in children after swallowing match heads is characterized by rather delayed (few hours) abdominal pain and vomiting. The vomitus has the odor of garlic and is luminous in the dark. Then there may be temporary recovery. After a few days, symptoms appear



FIG. 4.—Phosphorus necrosis of the jaw.

due to the degeneration produced by phosphorus in the epithelial and muscular tissues. Fatty degeneration results from diminished oxidation. The liver is especially involved and greatly enlarged. Marked jaundice occurs and hemorrhages into the skin. In fatal cases, there follow marked weakening of the pulse, delirium, coma and final collapse.

The chronic poisoning slowly induces the same epithelial degeneration in the glandular organs especially the liver and kidney. Red blood cells are destroyed, so that there results a state of chronic cachexia with emaciation, jaundice, anemia

and albuminuria. Workers in match factories are most exposed to chronic phosphorus poisoning. The poison may be inhaled in the form of fine dust. From the mouth it finds its way to the bone either through the pulp canal or some defect on the periphery of the tooth. In the bone an osteoporous necrosis is set up. The periosteum at first escapes serious injury. A sequestrum of spongy dead bone separates and sloughs out leaving an excessively foul cavity which has a very sluggish tendency to heal. A large part of both upper or lower jaws may be destroyed in this way (Fig. 4). In the lower jaw considerable new bone may be laid down by the remaining periosteum. This condition of "phossy jaw" as it is called in the match factories has been almost entirely eliminated by inspection of the mouths of all employes and by insisting on complete dental treatment of all carious teeth and diseased gums. The red amorphous phosphorus has also largely replaced the more volatile and poisonous white phosphorus.

Organic Poisons.—Organic poisons of infinite variety occur and their minute actions on living tissues are part of the subject-matter of pharmacology. All organic poisons, especially after long-continued action produce tissue degenerations in many instances identical with those of inorganic poisons or of any other intoxications including those of bacterial diseases. Herein lies the pathological significance of the study of poisons. As stated before the whole action of poisons exogenous and endogenous including the chemical and structural changes induced in the tissues comprises a large part of pathology. A few organic poisons of practical value may be considered as illustrative of the group.

Alcohol.—Alcohol is perhaps the commonest organic poison. It is the exciting cause of a great variety of pathological changes in the various systems of the body and a predisposing cause of acute and chronic infections, especially in tuberculosis and pneumonia. It has been an enormous sociological factor in the total morbidity of the working classes. The most direct effect of the ingestion of alcohol is seen from the use of concentrated alcoholic beverages. An acute gastritis may result with pain and vomiting similar

to the symptoms of the acute metallic poisonings. More often the habitual use of alcohol causes a chronic inflammation of the mucosa of the alimentary tract, especially of the pharynx, stomach and upper small intestine. This pharyngitis and gastro-enteritis causes serious impairment of digestion, loss of weight and also cough from the irritation of the throat. The clinical picture of such a patient is not unlike that of pulmonary tuberculosis and indeed the latter is frequently associated with chronic alcoholism. The throat inflammation extends in varying degree over the whole oral cavity, nasopharynx, larynx and trachea. The tongue is badly coated and pyorrhea frequent. Such mucous membranes pour out an abnormal amount of mucus. Hypersecretion will later be mentioned as one of the special characteristics of inflammation of mucous membranes. This condition of the throat is frequently called "catarrh" but this is no disease in itself. Catarrh is more often symptomatic of a general intoxication or gastro-intestinal disease than of any local condition in the nose or throat,

Pathological Changes due to Alcohol.—Alcohol or its by-products are absorbed in quantity into the portal circulation and produce fatty and other degenerative changes in the liver leading to extensive fibrosis or cirrhosis of that organ. Fibrous tissue is the most readily regenerated of all tissues and is found to fill in defects in the parenchyma of organs. All alcoholics will not develop cirrhosis of the liver but neither will all develop neuritis or any other one toxic result of alcohol. Other intoxications including infectious diseases may cause cirrhosis of the liver. This fact serves mainly to exemplify further the essential similarity of a great variety of poisons in their effect on pathological processes. Different individuals react differently to the same intoxications. Alcohol illustrates this very well. Different systems of the body bear the brunt of the poisoning. In some individuals the digestive system including the liver, escapes quite well, while the nervous system seems much more sensitive. Peripheral neuritis is usually the first manifestation, with a predilection for the lower extremity. "Toe drop" of alcoholic neuritis like the "wrist drop" of lead

neuritis is a common observation. Sciatic neuritis or the so-called sciatic rheumatism is often alcoholic in origin. Neuralgic pains about the jaws with or without tooth irritation, headache, backache, sleeplessness, tremor and a great variety of nervous symptoms result from the toxic hypersensitiveness of the nervous system. More severe intoxication leads to mental conditions—delirium tremens, alcoholic insanity and in extreme cases to a degree of nervous degeneration approaching that of paresis. Delirium tremens may be suddenly precipitated in a chronic alcoholic by an accident, especially with a fracture such as a fracture of the jaw or by an acute infection such as an abscess of the neck of dental origin or pneumonia. There is often a gross increase in the cerebrospinal fluid in these alcoholics—a condition known as “wet brain” or “serous meningitis.” From the diagnostic standpoint syphilis of the central nervous system must be constantly kept in mind as an etiological factor in the more severe nervous disturbances. As a rule the signs and symptoms due to alcohol and syphilis are distinctive, but at times are combined in the same patient. The dentist should keep in mind the possibility of these systemic diseases in a patient with trigeminal neuralgia and a mouth full of bad teeth. The vilest mouth may for a time at least produce no symptoms. Long standing alcoholism leads to mental and moral deterioration, which has been perhaps disproportionately associated with chronic drug intoxications, especially morphinism. The chronic drunkard can be trusted little more than the drug fiend and so far as gross tissue changes are concerned these may be much more easily demonstrated clinically and pathologically in alcoholism than in morphinism.

The circulatory system shows a slow degeneration after years of alcoholism leading to fibrosis of the myocardium (myocarditis) and enlargement of the heart and similar processes in the arterial walls (arteriosclerosis). Since the health of all the tissues depends upon the integrity of their arterial blood supply, arteriosclerosis may cause pathological changes in any part of the body. Alcoholism in this way favors premature senility and predisposes strongly to

terminal infections, especially pneumonia, erysipelas and septicemia arising from a focal infection such as abscess of the mouth or neck. A primary heart failure may also be the closing scene. Obviously the chronic alcoholic is not a good subject for general anesthesia. The kidney may be affected directly by the toxic action of alcohol or indirectly by arteriosclerosis of the renal vessels. Chronic nephritis is the rule in the old alcoholics. Acute nephritis is frequent following an acute alcoholic debauch, especially in association with an infectious factor such as tonsillitis or abscessed teeth. Alcohol has an inhibiting effect on ferments and vital cellular reactions especially of phagocytic cells toward bacteria. This combats the natural defense of the body in the acute infectious diseases. For this reason alcohol has little place in the treatment of these infections except in patients previously habituated to its use. Its former popularity was largely due to its antipyretic action and the general sense of well-being produced.

Methyl or wood alcohol, has a more toxic action than ethyl alcohol. The optic nerve endings are especially susceptible and complete blindness may result from moderate quantities. Larger amounts produce profound coma with dilated and absolutely fixed pupils. Such a patient may present the picture of apoplexy or meningitis. An epidemic of wood-alcohol poisoning with many deaths followed the establishment of prohibition in the United States.

Alkaloids.—The alkaloids are an important group of organic poisons with powerful effects on living cells, especially of the nervous system. Chemically they are nitrogenous bases capable of forming stable compounds with acids. As a group reaction alkaloids produce a primary stimulation followed by paralysis of the central nervous system. Cocain, morphin and strychnin may be considered as illustrative of the group.

Cocain is a general protoplasmic poison acting on all tissues. Locally it temporarily suppresses all cellular functions and produces anesthesia. Generally it typifies the alkaloidal group reaction of primary stimulation and in very large doses paralysis of the central nervous system.

Acute cocain poisoning is characterized by psychic excitation, restlessness, talkativeness, dilated pupils, accelerated pulse and respiration and choreiform movements, which with increasing dosage pass into general convulsions followed by collapse, coma, cyanosis and death by respiratory failure. The postmortem appearances are those of asphyxia. The limit of safety as to the amount of cocain used for local anesthesia is about 1 grain. Certain individuals have an idiosyncrasy for cocain and very rarely sudden death has occurred. However, a great many cases are reported as cocain idiosyncrasy which are ordinary fainting spells, psychic shock from pain or fear of pain, hysterical seizures or real shock from severe pain. Many such cases occur before injection of any cocain or even before the insertion of the needle and do not show the psychic stimulation at first and the succession of symptoms just described as typical of the absorption of toxic quantities of cocain. This is important for the dentist to appreciate since many unpleasant experiences may be avoided by the proper attitude toward and management of nervous patients. Some dentists have had as many accidents with the much less toxic derivatives of cocain such as novocain as with cocain itself. Chronic cocain poisoning will be described with chronic morphinism as the conditions are frequently associated and the effects essentially the same.

Morphin produces some stimulation of the central nervous system, especially in certain individuals, but the predominant action is a primary depression with progressive paralysis of the pain sense. Respiration becomes slow and shallow. The pupils are markedly constricted. Peristalsis is inhibited. Acute morphin poisoning is characterized by pin-point pupils, slow full pulse, flushed skin and shallow respirations which may be as infrequent as four a minute. The patient is roused with difficulty and with sufficient dosage of morphin, settles down into profound coma and dies from respiratory failure.

Chronic morphinism, or the habitual use of the opium derivatives, leads to profound physical and moral degeneracy. The digestive tract is first disturbed leading to alternating

constipation and diarrhea, anorexia and emaciation, The skin shows a curious, waxy pallor. Premature graying of the hair and lusterless, evasive eyes are quite characteristic. The higher psychical centers are particularly vulnerable to this type of poisoning. The typical drug fiend becomes hopelessly dishonest, unscrupulous and irresponsible, not only in methods of securing his drug but in all his personal relations. Nervous tremors and general irritability are usually present, but peripheral neuritis is less frequent than in alcoholism. Abstinence symptoms, catarrhal and nervous, are very marked in these cases when the drug is withheld. A very characteristic bluish, mottled pigmentation of the skin results from the habitual use of the hypodermic needle. Increased tolerance for morphin is acquired by the body and incredible quantities are reported as the daily dose of the confirmed habitu  . The usual amount taken is 5 to 20 grains a day. This intoxication is a strong predisposing cause of infectious diseases such as tuberculosis. Terrible as this picture is, morphin, properly used, is one of the most valuable and beneficent agents known to medicine. It is important to know that the morphinist is very inclined to ascribe his habit to the indiscretion of his physician or someone else. As a matter of fact many cases of morphin, cocain and heroin habit have originated in immoral associations the same as drunkenness. Patients do not acquire the habit from a few doses after an operation or fracture or at the height of a severe infection or hemorrhage. In many acute conditions, a full dose of morphin may be a life-saving measure. It is never justifiable to give a patient tablets to be used "as necessary" for chronic or recurring painful conditions. Chronic cocainism is said to lead to even more abject depravity than morphinism and to have more of a tendency to insanity and epileptiform convulsions.

Strychnin has a powerful influence on the nervous system by increasing its reflex excitability. Afferent impulses to the spinal centers lead to greatly increased efferent impulses to the muscles. The patient with strychnin poisoning may be thrown into general convulsions by a touch or a sound. The back is arched back in the position of opisthot-

onos as in tetanus and meningitis. Therapeutic doses act as a stimulant to respiration and all the vital functions by the same increased reflex excitability.

Poisonous Gases act very promptly, because absorption into the blood after inhalation into the lung occurs more rapidly than through any other channel. The toxic action on vital organs is produced in the same way as if absorption had been from the gastro-intestinal tract. There may also be marked local irritant action on the membranes. A third mechanism is by interference with the oxygen-carrying power of the blood, producing the so-called internal asphyxia. All of these actions were seen in one or other of the great variety of poisonous gases used in the great war.

Carbon Monoxide is the common cause of gas poisoning in civil life. It is contained in illuminating gas and especially in water gas. It is produced by incomplete combustion in stoves and in the exhaust of automobiles and other gasoline engines. Carbon monoxide is a colorless, odorless, non-irritating gas which has a great affinity for the hemoglobin of the blood. A firm chemical combination occurs which prevents the absorption of oxygen. A painless death quickly results from internal asphyxia. The poisoning is insidious and without warning. The victims may be found dead in a sitting position and with a very life-like pink in their lips. The color is due to the cherry-red carbon monoxide hemoglobin.

Carbolic Acid may be considered as an example of a large group of non-alkaloidal organic poisons. It is the best known of the coal-tar and benzene derivatives, which have certain group reactions in common. To varying degrees they are all analgesic, antipyretic, antiseptic or corrosive. In a general way these actions become less powerful as their chemical structure becomes more complex, that is more remote from the mother substance—benzene C_6H_6 or its first oxidation product, phenol or carbolic acid C_6H_5OH . Locally, carbolic acid in contact with the tissues produces a white, crumpled membrane which is anesthetic; and with prolonged action detaches at the edges or sloughs as a gangrenous mass. Carbolic gangrene is a well-known clinical

variety of gangrene, and numerous cases result from a lack of appreciation of the toxicity of this substance. It has practically been abandoned as an antiseptic dressing. Many cases of complete gangrene of a finger with spontaneous amputation have resulted from carbolic acid gauze dressings. If applied over a large surface or a carbolic solution is used for irrigation of an abscess cavity toxic amounts are readily absorbed. The general effect whether by absorption in this way or following the taking of carbolic acid by mouth is shown first by the dark, "smoky urine" so characteristic of this form of poisoning. The acid is excreted in the urine in the form of non-toxic phenol sulphonates. The smoky urine serves as a danger signal when carbolic acid is used. Large doses by mouth, as in suicide cases, produce very prompt collapse. Within a few minutes faintness and muscular weakness appear, then twitching and convulsions. The pulse is weak and slow, respiration slow and shallow. The patient rapidly passes into coma and dies from respiratory failure. The antidote is alcohol, which acts as a solvent of phenol. The mixture should not be left in contact with the tissues or in the stomach. The commonly used coal-tar analgesics such as aspirin, phenacetin, acetanilid, antipyrin, etc., while very valuable when used with discretion, share in mild degree the depressing influence on the pulse and respiration just described, and are best avoided in a patient who is making a close fight for life.

Finally, *ptomaines* represent a group of food poisons which have a profound effect on the body. The term ptomain was originally applied to definite alkaloidal substances produced by putrefaction, but has now been popularized and extended to mean any kind of food poisoning. Meat, milk, cheese and canned foods are the commonest sources of these toxic products. They are sometimes due to disease in the animals before slaughter and sometimes to bacterial infection, especially anaërobic (botulism), after the food is prepared. The latter poisons are thermolabile and can be destroyed by heating just before the food is eaten. This applies to the process of "cold pack canning" recently advocated as an economic measure. The *Bacillus botulinus*

or its spores may survive in food if the sterilization is not perfect. Many ptomaines are thermostable, however, and in the case of meat may not even affect the flavor. The usual symptoms are abdominal pain, vomiting and diarrhea and in many cases, symptoms suggestive of an atropin action such as dryness of the mouth, dilated pupils and rapid heart. There may also be paralysis, especially of the eye muscles and of the throat. Quite characteristic of botulism is the incubation period of twelve to forty-eight hours before the onset of symptoms. Some forms of ptomain poisoning are rapidly fatal. Chronic cases as in the prolonged ingestion of tainted meats show various tissue degenerations. In fact some regard this form of intoxication as a factor in the etiology of scurvy. It is important to know that the lay diagnosis of "ptomain poisoning" is often applied to cases of acute gastritis from overeating, especially of rich foods and combined with alcoholic beverages. Another source of diagnostic error is the onset of many acute infections with pain, vomiting and prostration. This applies to pneumonia, infantile paralysis, scarlet fever, erysipelas and other streptococcus infections and even severe tonsillitis. Gall-stone and kidney-stone colic and appendicitis may also be confused.

CHAPTER IV.

ENDOGENOUS INTOXICATIONS—BACTERIAL POISONS.

BACTERIAL action may result in the production of poisons without actual infection of the tissues. The contents of the alimentary tract are really outside the tissues of the body. A great variety of bacteria abound normally in the mouth and gastro-intestinal tract and aid in normal digestion. However abnormal types or numbers of organisms or retention of their products of growth lead to the absorption of poisons or as it is rather loosely termed "auto-intoxication." In marked constipation, indican, a derivative of indol, which is a direct product of proteid metabolism, can be readily demonstrated in the urine. This absorption of intestinal poisons is the most frequent pathology of the indefinite "biliousness" of the laity. Similarly oral sepsis and accumulated decomposing material even with intact teeth may lead to absorption of poisonous products and systemic disturbances.

Bacterial infection of tissues proper opens up the largest chapter of pathology and clinical medicine. Each pathogenic organism has its specific toxin and the body reacts in a specific manner to the toxin resulting in a great variety of pathological processes and clinical symptoms. The infection of Vincent's angina, for example, has mostly a local destructive action in throat with little systemic effect. Diphtheria, on the other hand, with a quite similar gross appearance of the throat lesion produces a most virulent toxin, which may poison and finally paralyze the heart muscle, or produce acute inflammation in the kidneys, or fatty degeneration in the liver. The specific bacterial toxins show a considerable degree of selective toxicity for

the various organs, or what comes to the same thing in clinical application, certain diseases have certain complications more frequently. Rheumatic fever commonly attacks the heart valves (endocarditis or valvular heart disease); scarlet fever more frequently the kidney (nephritis).

A very general classification of the pathogenic organisms will be of value in studying the rôle they play in pathological processes. Details and cultural characteristics, of course, are the subject-matter of bacteriology.

Vegetable Forms:

- I. *Cocci*—Ball-shaped, minute, non-motile organisms growing in a variety of forms.
 - Staphylococci*—grape-like clusters, commonly in localized abscesses.
 - Streptococci*—chains, commonly in spreading infections.
 - Pneumococci*—or *Diplococcus lanceolatus*—pointed paired forms, causing pneumonia.
 - Gonococci*—Biscuit-shaped paired organisms, causing gonorrhea.
 - Meningococci*—morphologically like, but culturally unlike gonococci, causing epidemic meningitis.
- II. *Bacilli*—rod-shaped, cylindrical forms, some motile, some non-motile, some spore-bearing, others not spore-bearing. As vegetable forms all divide by fission, that is at right-angles to their long axis.
 - Bacillus typhosus*—typhoid fever.
 - Bacillus diphtheriæ* of Klebs-Loeffler—diphtheria.
 - Bacillus tetani*—tetanus, or lockjaw.
 - Bacterium dysenteriæ*—Bacillary dysentery. The ending *ium* implies non-motility.
 - Bacillus influenzæ* of Pfeiffer—influenza.
 - Bacillus pyocyaneus*—green suppuration.
 - Bacillus aërogenes capsulatus*—gas gangrene. A great variety of other pathological bacilli.
- III. *Spirilla*—curved or spiral forms, usually motile and dividing by transverse fission as the other vegetable organisms.

Spirillum cholerae Asiaticæ—also known as the comma bacillus of Koch—cholera.

Spirillum Vincenti—with *Bacillus fusiformis*, Vincent's angina.

IV. *Actinomyces*—higher plant forms with branching filaments—non-motile.

Actinomyces bovis—actinomycosis.

V. *Fungi*, moulds and yeasts—more complex vegetable forms.

Oidium albicans—thrush (of the mouth).

Trichophyton—tinea (ringworm, barber's itch, etc.).

Sporotrichium beurmanni—sporotrichosis.

Streptothrix or *Nocardia*—Mouth and lung infection (streptothricosis).

Animal forms:

I. *Protozoa*—unicellular nucleated forms.

Entameba buccalis or *gingivitis*—possible cause of pyorrhea.

Entameba histolytica—amebic dysentery.

Plasmodium—malaria.

Spirochæta—syphilis.

The *spirochetæ* are spiral forms in which the longitudinal division and other characteristics of animal forms are questionable, so that some writers classify them with the spirilla under vegetable organisms.

Trepanosoma—African sleeping sickness.

II. *Worms*:

Nematodes—round-worms.

Oxyuris vermicularis—pin-worms.

Ascaris lumbricoides—round-worms.

Trichina—pork poisoning—trichinosis.

Ankylostoma—hook-worm.

Cestodes—tape-worms.

Tænia saginata—beef tape-worm.

Bothriocephalus—fish tape-worm.

III. *Arthropods*:

These higher forms act mainly as intermediate hosts—in carrying pathogenic organisms.

Insecta:

Pediculus capitis—head lice.

Pediculus corporis—body lice—carries the infective agent of typhus fever.

Cimex—bed-bug—may carry the *Bacillus pestis* of bubonic plague.

Stegomyia and *Anopheles*—mosquitoes—the latter carries malaria and the former yell ow fever.

Acarus scabiei—carries scabies or common itch.

The Relation of Bacteria to Disease.—The mere presence of a microörganism in the lesions of a disease does not necessarily mean that the organism is the specific cause of the disease. Innumerable saprophytic organisms abound on the surface of the body and in the gastro-intestinal tract. Bacteria also have a considerable capacity for adaptation to environment so that abnormal types are developed in the body or in the lesions of a disease because of abnormal chemical or physical conditions. Such organisms may be associated with a disease in a very characteristic way and yet bear no causal relation to the disease. In order to establish the etiological relation between an organism and a disease certain conditions must be fulfilled, which have been formulated under the following four laws of Koch:

1. The organisms must be obtained from the diseased individual.
2. The organisms must be cultivated on media outside the body.
3. Pure cultures injected into healthy individuals (animals) must reproduce the disease.
4. The organism must be recovered from the tissues of the individual thus infected.

The infectious diseases are said to be *epidemic*, when prevailing at a certain time; *endemic*, when prevailing in a certain locality; and *pandemic* when prevailing universally as the pandemics of influenza in 1893 and 1918 and 1919, which went around the world.

The portal of entry or atrium of infection in these diseases is the point or channel through which the organism gains

entrance to the tissues. The following examples illustrate how the body is open to attack in all quarters:

1. *Skin*—through hair follicle—pimples, boils, carbuncles, through puncture wounds, abrasions, etc.; tetanus, erysipelas, syphilis, etc.; through intact skin occasionally.

2. *Oral cavity*—dental and tonsillar infections which may extend through the deep veins to the intracranial venous sinuses causing thrombosis or brain abscess—also diphtheria, Vincent's angina, syphilis, neck abscesses and infections of the jaws.

3. *Nasal cavities*—common colds—cerebrospinal meningitis, by extension through the cribriform plate of the ethmoid to the meninges.

4. *Respiratory tract*—pneumonia, tuberculosis, influenza.

5. *Gastro-intestinal tract*—typhoid, dysentery.

6. *Genito-urinary*—colon bacillus infections, pyelitis, venereal infections, gonorrhea, syphilis, postpartum infections, septicemia.

CHAPTER V.

RESULTS OF BACTERIAL INFECTIONS.

THE results of bacterial infection may be studied further by following up the action of the common pyogenic cocci, staphylococcus and streptococcus. When these organisms are introduced into the tissues, as, for example, by extension through a carious tooth and root canal to the periapical tissues, they multiply and liberate toxins as a result of their growth. These toxins injure the tissues and result in inflammation, the detailed process of which will be studied later. Inflammation, however, is a defence reaction, and if it proves inadequate to the invading organism the infection extends. General symptoms result which are of great practical importance. There are three fairly definite stages in the process—toxemia, septicemia and pyemia.

Toxemia (toxins in the blood) or sapremia is the absorption of toxins from a localized infection into the blood. Sapremia is sometimes applied to the absorption of non-bacterial products such as sterile blood clot after an operation. The symptoms of toxemia may be very severe and serve as a guide to the extent and virulence of the infection. Fever is the main manifestation of the body reaction to toxemia. Fever may be of three types—continuous, remittent or intermittent. Continuous fever progresses at a constant or nearly constant temperature level. Remittent fever shows daily drops in temperature but not to normal. Intermittent fever drops daily from a high temperature to normal or subnormal level. Toxemia shows a continuous or remittent type of fever of 100° to 104° . Other symptoms are associated—headache, anorexia, thirst, muscular aching and general malaise. Delirium may occur in the severe forms. If the toxemia is prolonged, various tissue degenerations may result, such as cloudy swelling and fatty degeneration.

Septicemia or Bacteremia (bacteria in the blood) is the more advanced condition in which both toxins and bacteria find their way into the circulating blood. This may be demonstrated by blood culture (1 c.c. of blood aspirated aseptically from a vein and incubated with 50 c.c. of bouillon). The symptoms are those of toxemia in more severe degree and fever of the intermittent or so-called septic type. Chills with the rise in temperature and sweats with the drop in temperature are frequent. The septic patient shows a brown coating on the tongue often dry and with a red tip. Jaundice, vomiting, delirium, and muscular twitching are frequent. A tendency to hemorrhage (acquired hemophilia) results in certain cases. Notable among these are the infections by the *Streptococcus hemolyticus* arising from blind abscesses at the roots of teeth. Many of the cases of so-called cryptogenetic septicemia in which the source of the infection is unknown are really of dental origin. Blood is laked by the toxins of the hemolytic streptococcus and hemorrhages result into the skin (petechiæ), the mucous membrane of the mouth in the form of bleeding gums, also in the gastro-intestinal and urinary tracts with the passing of blood. An extraordinary degree of anemia is seen quite frequently in "septic" cases. The heart valves flapping incessantly in the bacteria laden blood stream are sooner or later attacked, causing an endocarditis, the commonest complication of septicemia. Virulent pyogenic septicemia is almost uniformly fatal. However, the routine use of blood culture in supposedly localized infections shows that organisms frequently find their way into the blood stream. The clinical picture of septicemia results when the generalizing infection is unchecked. Certain bacillary infections such as typhoid fever show a bacteremia as the essential pathology of the disease. The prognosis of septicemia due to the pyogenic cocci, however, is bad and the great practical importance of this fact to the dentist cannot be overemphasized. Early and free drainage is the great preventive treatment of abscesses that threaten to generalize. Unnecessary tearing open of lymph spaces as in the extraction of a tooth is not devoid of danger in the presence of an acute

infection. When practicable, simple incision and drainage of an alveolar abscess and subsequent extraction of the tooth is better than primary extraction, especially in an old or debilitated patient. No surgeon would think of removing tonsils during an acute attack of tonsillitis. Some of the cases of uncontrollable hemorrhage following extractions encountered by dentists are really septic cases. Particular caution is indicated in the case that is referred to the dentist for treatment on account of anemia due to oral sepsis. A septicemia may already be under way and an acquired hemophilia established. For serious hemorrhage, serum injections and blood transfusion are necessary as well as local hemostatic measures.

Pyemia (pus in the blood) is not literally pus in the blood but the final stages of generalized infection, in which secondary or so-called metastatic or pyemic abscesses arise in various regions of the body as a result of circulating bacteria or infected particles such as detached blood clots from the primary focus of disease. A suppurating focus about a vein may lead to infection and clot formation (thrombophlebitis) within the vein. Such a septic thrombus may be a prolific source of infected material constantly or intermittently discharging into the blood stream. When the heart valves are involved (septic endocarditis) as is frequently the case, infection is disseminated similarly through the arterial system (arterial pyemia). Detached particles (emboli) obviously may lodge anywhere in the body. The local symptoms depend upon the organ involved. The general symptoms are similar to those of septicemia—intermittent fever, sweats, chills, jaundice, anemia and eventually emaciation and profound exhaustion. The cases may go on many months and finally succumb, although occasionally recovery occurs in apparently hopeless cases. Pyemic abscesses may be localized in any organ but are more frequent in joints such as the hip, knee and jaw-joints—also in the bone-marrow (osteomyelitis), lungs, serous cavities and kidneys. The parotid is a common site for metastatic abscess. Blood-borne infection may even lodge in the center of the eye or the pulp of a tooth. With reference to dental

infections, however, the sequence is far more frequently reversed. The atrium of infection is the tooth—then an apical abscess—then an osteomyelitis of the lower jaw or an antrum infection in the upper jaw, possibly a thrombosis of the intracranial venous sinuses, then a septicemia or pyemia. Other sources to be considered in an obscure pyemia are suppuration in the tonsils, sinuses, middle ear, cavities in the lung, gall-bladder, appendix, Fallopian tubes and prostate.

Localized Coccus Infection.—*Staphylococcus infection* is the common skin infection in furuncles and carbuncles also in the superficial suppuration of impetigo contagiosa, which is very frequent about the mouth and face. Impetigo may be the atrium through which staphylococci gain entrance to the circulation. *Osteomyelitis* is one of the most characteristic of staphylococcus infections. The localization of the organisms is frequently determined by a contusion, fracture or some process lowering the local resistance to infection. Diseases lowering the general resistance also favor osteomyelitis and definite areas of degeneration may be found in the bone-marrow following such diseases as scarlet fever and diphtheria. When staphylococci gain entrance to the medulla, the cancellous bone tissue inflames and suppurates. The process extends to the compact bone a mass of which may be detached as *sequestrum* of dead bone lying in the cavity of the enveloping *involucrum* of normal bone. Overlying this the periosteum is elevated and infection extends through into the muscles and adjacent soft parts. The joint in long bones is frequently involved because the epiphyseal line, where new bone is being formed is the most susceptible to the staphylococcus infection causing osteomyelitis. In the jaw staphylococci may extend directly from an infected root of a tooth into the bone and lead to sequestrum formation. In chronic cases a secondary deposit of very dense bone (eburnation) results, so that the mandible will keep its form after the removal of a sequestrum nearly the original size of the bone.

Streptococcus infection is one of the most important of all types of bacterial disease to the dentist because of its fre-

quency in relation to the oral cavity and because of the tendency to spread through lymphatic channels or to generalize as a septicemia. The local reaction to the streptococcal toxin is not such as to limit the process within an abscess wall as is characteristic of staphylococcus infection. From the primary atrium of infection, red streaks of lymphangitis indicate the early extension, so that the regional lymph glands may show the first symptoms of inflammation of any severity. A puncture wound in the finger, for example, with virulent streptococci introduced may result in an axillary abscess. Similar infection at the root of a tooth very readily extends through the abundant lymphatics of the neck to produce diffuse suppuration. This sometimes results in an extraordinary board-like induration of the neck known as Ludwig's angina, which may be rapidly fatal unless treated by early and free drainage. In a child inflammation in the region of the larynx readily leads to edema of the glottis with the danger of suffocation. The infection is disseminated along the planes of the cervical fascia to the root of the neck and mediastinum. The tension may be so great as to result in extensive sloughs. The infiltration may involve the floor of the mouth, causing difficulty in opening the mouth or in swallowing. An unerupted third molar may be the portal of entry as well as the ordinary carious tooth or peritonsillar abscess.

Streptococcus infection may be non-suppurative as in the common throat infections and erysipelas. Tonsillitis is usually a streptococcus infection. Such infection frequently extends to the middle ear and mastoid and occasionally to the meninges and brain. In severe tonsillitis numerous streptococci escape into the blood stream and may cause an endocarditis, arthritis or nephritis. The nasopharyngitis of head colds is a similar infection, sometimes streptococcus, sometimes pneumococcus and other organisms but head colds are always typical infections, although predisposing causes play a large part in their etiology. Organisms are frequently harbored in the throat, in the crypts of the tonsils or in the accessory sinuses of the nose, to break out in active form when the resistance is lowered by exposure.

This has occurred on a large scale in the recent pandemic of influenza. Dentists may easily take colds from patients or as easily infect patients. Dentists should also remember that infections of the antrum of Highmore are more often due to nose colds than to dental infections and that when of nasal origin they may cause neuralgic pain in the upper teeth because of the relation of the upper dental nerves to the floor of the antrum.

Erysipelas.—Erysipelas is an acute contagious, usually non-suppurative and self-limited inflammation of the skin and subcutaneous tissues or mucous membranes, with marked constitutional disturbance. It is due to a streptococcus, which spreads rapidly in the lymph spaces and around the bloodvessels. Lymphocytes are the chief type of cell seen in the inflamed tissues. The infection starts practically always in some defect in the skin or mucosa and in a majority of cases in relation with the nasal or oral cavities. It may start at the ala nasæ, spread across the face, ear, scalp and completely encircle the head. It may begin within the antrum and indeed originate from an abscessed tooth and produce an obscure fever until the eruption appears at the nostril. Incisions into infected mucous membranes such as in operations on the mastoid or the maxillary antrum or the extraction of an abscessed tooth may be the starting-point of erysipelas. It appears as a tense, bright red eruption, with an elevated, advancing irregular margin. The older area fades as the brighter edge advances. Small vesicles form over the tense swollen skin and in severe cases coalesce to form large bullæ. Loose and lax tissues such as about the eye are greatly swollen and the features distorted. There is high fever promptly at the onset, often with chill, vomiting and prostration in severe cases. The fever usually runs a remittent course of four to six days and ends sharply by crisis, although milder cases frequently defervesce by slow lysis. The swelling of the parts lingers quite persistently in many cases and after repeated attacks, which occur in susceptible individuals leads to a permanent edema. A certain amount of pigmentation also remains for a considerable period. Alcoholism and

chronic disease are strong predisposing causes of erysipelas and the largest factor in the prognosis. The young and vigorous patient usually recovers, the weak or aged patient frequently succumbs. The complications are the same as other forms of streptococcus infection, most commonly, nephritis, endocarditis and septicemia.

Phlegmonous erysipelas is an atypical form in which the infection extends to the deeper tissues and regional lymph glands and results in suppuration. This requires incision and drainage, the same as any abscess. Cutaneous erysipelas never requires incision. In fact local treatment of any kind is of secondary importance. Measures to check the advancing border are usually of no avail. A saturated solution of magnesium sulphate externally, probably by an exosmotic action, reduces the hyperemia and tension of the tissues.

Scarlet Fever.—The streptococcus throat infections are very closely related to scarlet fever. It is doubtful whether there is any other specific organisms as the cause of the disease. Atypical forms of scarlet fever occur under a variety of conditions in which streptococcus infection gains entrance. After removal of tonsils, after dental operations or any surgical operation, the so-called surgical scarlet fever occasionally occurs. The streptococcus may gain entrance in association with other organisms, especially in the throat. Diphtheria and scarlet fever coëxist not infrequently. A certain proportion of the epidemic influenzal cases have developed scarlet fever rashes followed by desquamation. The suppurative complications of scarlet fever, such as abscesses in the ears and neck are usually due to the streptococcus. On the other hand so-called true scarlet fever shows certain distinctive clinical features such as the short incubation period, the sudden onset and the subsequent immunity which are strongly suggestive that there is a specific etiological agent in the disease. It is possible that it is only a particular strain of streptococcus, analogous to the streptococcus of erysipelas. There are no characteristic pathological lesions of scarlet fever other than streptococcus infection and the skin eruption.

The reddened throat is of a particularly scarlet hue and the tongue shows enlarged papillæ, giving the appearance of the "strawberry tongue." The toxin of the disease has a selective affinity for the kidney cells, so that acute nephritis (Bright's disease) is a frequent complication. In any event the quarantine and practical management of all cases must be the same in order to safely control contagion. From the dental standpoint this is a very important consideration. It means that epidemic sore-throat is a potential source of scarlet fever and other diseases. These cases are a real danger to dentists and to other patients.

The simple coccus infections illustrate sufficiently the etiological relation of organisms to pathological processes and clinical symptoms. Later under the head of special infections the reaction to other types of bacterial invasion will be considered. A group of chronic infections, the infectious granulomata, may be considered as intermediate between inflammatory processes and true tumors, since they are characterized by a marked overgrowth of new tissue. They include the following: tuberculosis, syphilis, actinomycosis, leprosy, glanders and rhinoscleroma.

CHAPTER VI.

ENDOGENOUS INTOXICATIONS—METABOLIC CAUSES OF DISEASE.

Faulty Food and Metabolism.—Metabolism includes the whole of the internal chemistry of the body. A very complex succession of chemical processes necessarily intervenes between the breaking down (katabolism) of food substances and the building (anabolism) of the protoplasm of living cells. The three fundamental food principles, proteid, carbohydrate and fat may be taken as the starting-point in the study of disease due to disordered metabolism.

Proteid Metabolism.—Proteid as the only nitrogenous food principle is essential to life. About 85 per cent. of the nitrogen of ingested food is excreted through the kidney in the form of urea. The nitrogen of tissue waste is excreted largely as uric acid in the urine. Consequently the function of the kidney is closely related to proteid metabolism. When the kidneys are damaged, as for example, in acute nephritis complicating a streptococcus infection of the mouth, functional rest may be afforded the kidney by withholding proteid food, especially meats. Vicarious elimination through the skin may also be favored by hot packs, since urea is excreted to some extent through the sweat-glands. Albumin is present in the urine at the height of the fever of almost any toxemia. The products of incomplete proteid digestion may be of the most poisonous type in addition to adding to the work of the kidney so that a low proteid intake is usually advisable for the toxic patient.

Derangement of Proteid Metabolism.—*Gout* is a disease of the proteid metabolism, one feature of which is an excess of uric acid in the circulating blood. It is characterized by attacks of acute arthritis and the gradual deposition of

needle-shaped crystals of sodium biurate (tophi) in and about joints and by the general symptoms of an intoxication (Figs. 5 and 6). Alcohol is the most potent factor in the etiology of gout. Sedentary life and an excessive meat diet are important associated factors. Bartenders and brewery men are usually familiar with the clinical picture of gout from seeing cases among their numbers. However,

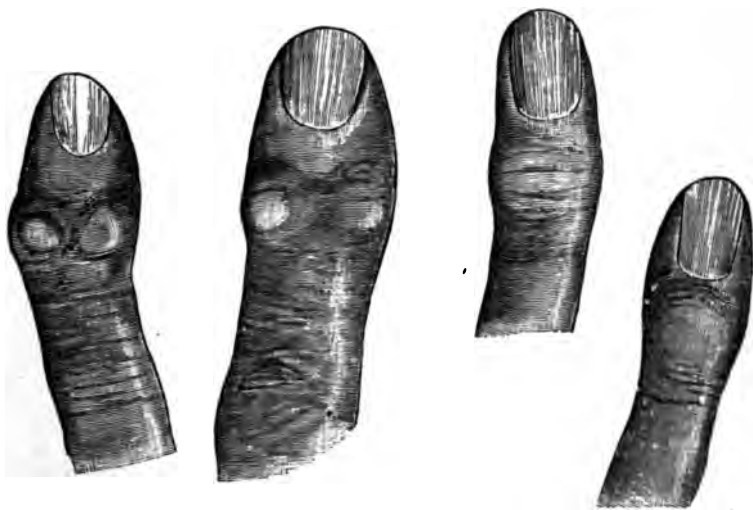


FIG. 5.—Heberden's gouty nodes. Illustrating common forms of terminal phalangeal deflection. Forefinger and little finger of a woman aged seventy-years. "Crab's-eye" cysts over the joints are also depicted. (Duckworth.)

FIG. 6.—Nodular swellings (Heberden's nodes) due to gouty arthritis on the forefinger and little finger of a woman aged fifty years. (Duckworth.)

there is a hereditary tendency to gout in certain families, many members of which may develop gout with little or no alcoholism. These are usually large, robust, full-blooded individuals, with quite luxurious habits of eating and living. As stated before lead poisoning resembles the toxic action of alcohol in several respects and may take the place of alcohol in the etiology of gout. Painters and lead workers

have long been known to be subject to gout. The exact nature of the metabolic defect which permits of this deposit of urates is not known, but all the predisposing factors tend to inhibit oxidation. Alcohol checks ferment action, which presides over most metabolic processes. Lack of exercise and overeating favor incomplete oxidation. Gout usually does not manifest itself before thirty-five to forty years of age, when the processes of oxidation and detoxication are less active. However, it may occur in childhood in families with a markedly gouty diathesis. Uric acid is not excreted in the normal amount for a period before an acute attack of gout. After the attack has begun there is an abnormal amount of both uric acid and phosphoric acid in the urine. The faulty metabolism is a constant condition, but the exacerbations are periodic and may depend on a variety of exciting causes. Nerve strain or a sudden mental shock may precipitate an attack—also an accident or operation. The extraction of a tooth may be followed the next morning by an attack of gouty inflammation in the great toe. An alcoholic bout also frequently is the determining factor in an attack.

Dental Aspects of Gout.—It would be well for the dentist to be familiar with the picture of acute gout, so that he may differentiate it from infectious arthritis or at least to know that there are other causes than dental and other focal infections for acute joint inflammations. The type of patient and the localization in the metatarsophalangeal joint of the big toe should always suggest gout. The attack begins usually in the night or early morning with agonizing pain in the joint and a sensation of pressure as if the toe were being squeezed in a vise. There are local heat, a tense shiny swelling and acute tenderness on the least motion. There may be fever of 102° or 103°. The attack lasts six or eight days with the pain usually more aggravated at night. Suppuration never occurs. At onset there may be an acute stomatitis and a distinct sore-throat. This oral manifestation of the acute phase of the gouty intoxication helps to explain the association of persistent pyorrhea in chronic gout. No more intractable forms of pyorrhea are ever seen

than those depending on severe metabolic diseases. Treatment directed toward the general condition is of more avail than any local measures. A gouty parotitis is said to occur occasionally. Chronic gout leads to a variety of degenerative conditions, chief among them being arteriosclerosis, chronic nephritis and high blood-pressure.

Disturbance of Carbohydrate Metabolism.—*Diabetes* is a disease depending upon the breaking down of the carbohydrate metabolism. Carbohydrate is the great energy-producing part of food substances. It is normally oxidized to carbon dioxide and water, yielding the same energy as if directly burned. Sugar and starch are important in the dietary of men doing hard, physical work, especially when exposed to cold. Experiments devised to collect and measure the carbon dioxide and water of the expired air of men doing a measured amount of physical work show a direct relation between energy output and carbon dioxide excretion. Obviously, if the carbohydrate digestion breaks down and sugar is eliminated unchanged in the urine, as occurs in diabetes, there is a great loss of energy and heat in the organism and clinically the patient shows a rapid loss of weight and strength. The exact etiology of diabetes is unknown, but a number of predisposing causes are definitely recognized. Heredity and race play important rôles. Jews are more frequently affected than other races. Obesity, profound nervous disturbances and injuries and diseases of the brain and spinal cord are at times direct antecedents of diabetes. Overindulgence in food and drink and a sedentary life favor diabetes, but the most severe cases come on without apparent cause in earlier life. The lowered sugar tolerance of hyperthyroidism or exophthalmic goiter sometimes passes over into true diabetes. Structural changes are found in many cases in the pancreas, although a considerable proportion of cases show no lesions whatever. The islands of Langerhans have frequently been found atrophic. In the slowly developing diabetes of advanced life an extensive fibrous or fatty degeneration of the pancreas is frequently found but the etiological relation of these changes to diabetes is not clear. Whatever the precise mechanism, dia-

betes represents a failure of carbohydrate metabolism. In bad cases, the so-called absolute diabetes, all sugar ingested passes through into the urine often in a concentration of 6 or 7 per cent. At the onset of the disease, there is loss of weight equalled only by that of tuberculosis and cancer. There is great thirst due to the excess of sugar in the blood (hyperglycemia). Gallons of water are taken and passed daily.

Dental Aspects of Diabetes.—The dehydration of the body leaves a characteristic dryness of the skin and mucous membranes. The gums become swollen and pyorrhea frequently progresses till all the teeth have loosened and fallen out. Inordinate appetite is the rule so long as the sugar content in the urine (glycosuria) is high. Excess sugar (over .12 per cent.), and other abnormal metabolites in the blood, constitute a toxemia and toxic pains are frequent. A frank diabetic neuritis in the latter stages of the disease may lead to marked loss of muscular power. The toxic state of the diabetic causes extreme lowering of the general resistance, especially to various bacterial infections. Boils and carbuncles are very common. Postoperative infections are frequent. Pneumonia, erysipelas or tuberculosis may carry off the patient. Sooner or later coma supervenes, due to the presence of acid bodies (diacetic acid, acetone, etc.) in the blood (acidosis). The breath has a heavy sweetish or fruity odor due to acetone. Coma is the most common terminal event in diabetes. It may be precipitated by a sudden shock, such as an operation, especially with general anesthesia. This accident can be guarded against to some degree by first rendering the patient "sugar free" by fasting and by the administration of a large amount of alkali, such as sodium bicarbonate.

Chronic diabetes leads to degenerative changes as with other intoxications. Arteriosclerosis may be extreme and with the toxemia may cause gangrene usually of the feet, but occasionally of isolated areas of skin such as of the neck. High blood-pressure is frequent in the older cases. Nervous degenerations occur oftener than in gout. The undermining of the general resistance is so marked that diabetics are notoriously bad operative risks. It should be stated, how-

ever, that cases which develop insidiously late in life are of a relatively benign type.

Other Metabolic Diseases.—*Scurvy* or *Scorbutus* is a metabolic disease not from derangement of any one of the primary food principles but in all probability due to the absence of certain substances (vitamins) in the diet. It has been the scourge of sailors for centuries, especially when they were deprived of fresh fruit and meats for long periods. Now the disease is controlled in the marine service by the compulsory use of limes at certain intervals on shipboard. The disease is also prevalent among prisoners of war and occurs in sporadic form in civil populations, especially in the foreign sections of large cities. Poor hygienic surroundings are a predisposing cause but a diet of canned goods without fresh fruits, vegetables and meats is the main etiological factor.

Oral Lesions of Scurvy.—The most characteristic lesions of scurvy are in the mouth. Spongy, swollen, bleeding gums, which in extreme cases may appear as fungous ridges on either side of the teeth as broad or broader than the occlusal surface of the molars. The gum may be swollen to such an extent as to be on a level with the occlusal surface of the molars and give the appearance at a distance of three parallel rows of teeth. The tongue is red and swollen and the breath foul. Oozing from the gums and hemorrhages under the oral mucous membrane are common. The teeth may loosen and fall out. Rarely there is necrosis of the jaw. The salivary glands are occasionally enlarged. The general symptoms are anemia, hemophilia, progressive weakness and emaciation. Hemorrhages into the skin (purpura) are frequent, especially over the shins. There are no characteristic visceral lesions other than hemorrhages into the various organs and serous cavities. Recovery is rapid and complete on suitable diet. The scarred gums may be seen throughout life, as for instance, in the survivors of Andersonville prison and in other aged Civil War veterans. From the standpoint of differential diagnosis it is important to keep in mind that purpura and an acquired hemophilia, including bleeding gums, may be due to septicemia and frequently of dental origin.

Infantile scurvy (Barlow's disease) is a much more prevalent condition at present than the adult form. Infants on proprietary foods or condensed milk are subject to it and for this reason it may occur in spite of otherwise good hygienic surroundings. The spongy gums occur if the teeth have erupted, but the characteristic lesion of infantile scurvy is subperiosteal hemorrhage, causing painful swellings on the shins and epiphyseal softening (pseudoparalysis).

Metabolic Diseases of Bone.—*Rickets* or *Rachitis* is a metabolic disease of infants characterized by impaired nutrition, lowered resistance, epiphyseal enlargement of bones, imperfect ossification and delayed dentition. It occurs in all parts of the world among children living in poor hygienic surroundings and is especially frequent among the children of the negro and Italian races. Like scurvy, the disturbance is probably due to the absence of certain necessary substances or vitamins in the diet. The precise nature of these substances is not known, but the diet on which rickets most commonly develops is deficient in both animal fat and proteid. There is also a faulty assimilation of lime salts. A cushion of cartilage between the shaft and epiphysis of long bones develops, producing a soft swelling, especially at the wrists and the junction of the ribs with the costal cartilages at either side of the sternum (rickety rosary) (Fig. 7). There is marked hypermia of these cartilaginous overgrowths and of the adjacent periosteum and bone. The calcium-content of these tissues is low—at times one-fourth the normal. In the skull, there result delayed closures of the sutures and fontanelles and bony thickenings in the center of the frontal and parietal bones giving a rectangular contour to the head and undue prominence to the sutures (hot cross-bun head of rickets). The head is large and the maxillæ underdeveloped. The teeth appear late and may be small and badly formed. Caries occurs readily. Spinal curvatures are frequent. Rickets is the common cause of bow-legs and knock-knees. Partial or green-stick fractures are not uncommon in the soft bones of rickets. The disease comes on about the period of dentition with slight fever, moderate anemia and impaired nutrition. It is never fatal alone but



FIG. 7.—Rachitis. Showing the cuboidal shape of the head, the thoracic deformity, the beaded ribs, the protuberant abdomen, and the enlarged lower end of the radius. (Koplik.)

predisposes strongly to intercurrent infections, especially pneumonia. Active rickets runs a self-limited course, subsiding in a year or two, although there are rare cases of so-called "late rickets" in children eight or ten years of age. Marked bony deformities, of course, are permanent.

Achondroplasia is another disease of bone, especially of the epiphyseal cartilages of the long bones. There is a failure of the normal growth of the long bones due to a premature union of the epiphysis with the shaft. Consequently the

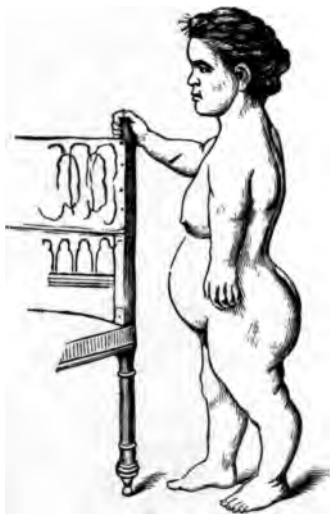


FIG. 8.—Achondroplasia. (Lugeol.)

subjects are of small stature and are known as achondroplastic dwarfs. The root of the nose is depressed. Otherwise the head and trunk are normal. The main shortening is in the humerus and femur (Fig. 8). The etiology of achondroplasia is not known, but there is some evidence that it is connected with disturbance of the pituitary gland (Fig. 14).

Fragilitas Ossium is a curious abnormality of bone, in which fractures occur with very slight violence. The jaw may be fractured while chewing. As many as a hundred

fractures have occurred in one patient. The fractures may be painless and may heal readily. The condition may be present at birth as an imperfect osteogenesis or it may come on later in life.

Food Deficiencies.—Vitamins or substances necessary for the normal metabolism have been the subject of recent pathological research. Two other diseases, beri-beri, and pellagra seem to be due to food deficiencies. In the former the vitamins apparently occur in the bran or polishings of rice, since the disease does not occur with a diet of unpolished rice and indeed may be cured by the administration of an extract of rice polishings. Pellagra now widely prevalent in southern United States is connected, though less definitely, with defective corn. It is quite possible that vitamin pathology may be widely applicable to the metabolic diseases.

Faulty Functioning of Organs.—Faulty functioning of individual organs necessarily leads to derangement of metabolism, the particular form of disturbance depending on the physiological function of the organ involved. Degenerations of various kinds may develop in the parenchyma of the visceral organs. With advancing age hardening and thickening of the arteries result (arteriosclerosis). This leads to progressive impairment of the circulation which involves every organ in the body. The kidney may be taken as an example. These changes constitute chronic nephritis or chronic Bright's disease. There is a gradual atrophy of the secreting structures, glomerular and tubal. Inevitably a state of toxemia develops due to the retention of products which should be excreted and especially to the by-products of an abnormal metabolism. This toxemia causes the well-recognized clinical condition of uremia. The cerebral symptoms are important and severe—headache, delirium, convulsions, paralysis and coma. Dyspnea and gastro-intestinal disturbances are frequent and as in most toxemias, there may be marked oral manifestations. A special uremic stomatitis has been described characterized by red, swollen lips, gums and tongue. The breath is excessively foul both from the toxemia and from local accumulations of sordes. Speaking and swallowing may be difficult. *Uremia* is the source of

a good many diagnostic errors. It has been confused with meningitis, apoplexy, alcoholism and infectious diseases, such as typhoid fever. Obviously, an old person bordering on uremia would be a bad operative risk. Resistance to infection is at a minimum. Dental conditions are practically always associated with infection and adequate drainage should be the first indication to be met. The chronic abscessed tooth should be extracted. The acute abscess should be incised and drained before extraction in order to avoid opening up tissue spaces to spreading infection.

Faulty Internal Secretions.—Finally metabolic disease may arise from faulty internal secretions. The endocrine glands, thyroid, parathyroid, adrenals, pituitary, pineal, thymus, the sexual glands, as well as the internal secretions of glands with duct systems such as the pancreas, have been the subject of extensive research during recent years. It is one of the growing fields of physiology and pathology. Although the functions of these internal secretions are not clear in many details, it is established beyond doubt that they exert a tremendous regulatory influence on bodily processes in health and disease. They have also been found to be very closely interrelated in their functions, "interlocking glandular directorates," as they have been called. Many clinical examples of disordered internal secretions are obviously pluriglandular in origin—curious mixtures of disturbed functions, a fact which has made exact knowledge difficult to obtain. No two cases of so-called dysendocrinism are alike. However, in many cases one type predominates, so that from these, as well as from animal experimentation, considerable knowledge has been gained, especially in connection with the three main glands—thyroid, adrenal and pituitary.

Thyroid Disturbances.—The thyroid shows two opposite types of disturbances, which may be regarded at least for the present simply as increased and diminished secretion—hyperthyroidism and hypothyroidism. As a matter of fact exophthalmic goiter is a more complex process than pure hyperthyroidism, but its exact nature is not fully understood.

Excessive Thyroid Secretions.—*Hyperthyroidism, exophthalmic goiter, Basedow's or Graves's disease* is now a well-known

clinical picture. The thyroid gland is enlarged and very vascular, and usually shows on histological examination a marked overgrowth or hyperplasia of the secreting epithelium. The exact etiology is not known, but various intoxications, infectious and otherwise, and prolonged nervous stress, play an important rôle. The cardinal symptoms are exophthalmos, tremor, tachycardia and the goiter (Fig. 9).



FIG. 9.—Exophthalmic goiter. (Meltzer.)

The wild, bulging eyes, the pulsating neck, the flushed, tremulous face and hands and the rapid, forcible heart action, apparent through the clothes, make the condition recognizable at a glance. The circulatory disturbance is profound. The pulse-rate may be 180 or 200—the blood-pressure elevated in systole to 180 or 200 mm. of mercury.

There is extreme vasomotor relaxation, with flushing, excessive perspiration and paresthesia of the skin surface. The heart may dilate under this abnormal drive of the circulation. Considerable emaciation is the rule, at times, twenty to forty pounds loss of weight. Metabolism, especially of carbohydrates, is greatly disturbed. Sugar tolerance is low. Glycosuria is frequent and occasionally genuine diabetes supervenes upon the metabolic break-down of hyperthyroidism. The nervous excitability of the patient is exaggerated

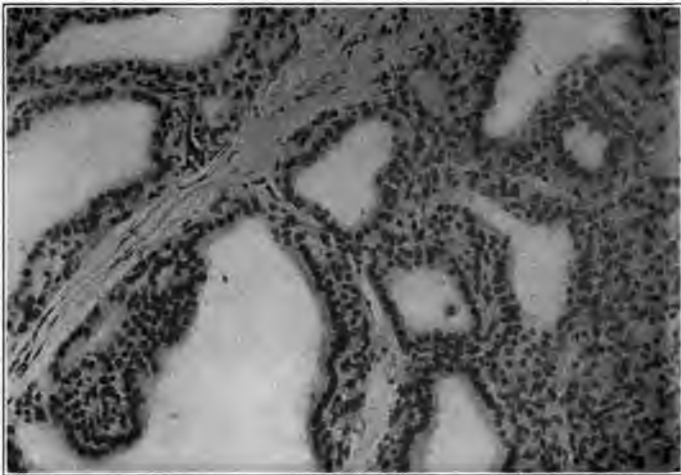


FIG. 10.—Hyperplasia of the thyroid gland.

both to reflex stimuli and emotional states. Sudden death from slight shock has frequently occurred. Surgical risks are greatly increased. The pain and fear of extraction of a tooth might cause serious collapse. It is important in the management of these cases that there be no period of anticipation of any operative procedures. Morphine in advance is advisable. "Stealing" the gland is sometimes practised, when thyroidectomy is to be done, by slowly starting nitrous oxide anesthesia without the patient's knowledge. In this way the tremendous acceleration of the

pulse and nervous upset of the patient are avoided. Removal of part of the thyroid is usually followed by definite improvement, but a long period of rest treatment is necessary for full convalescence. Mild cases will recover without operation. Some types of so-called nervousness are really cases of mild hyperthyroidism. They probably make up some of the dentist's cases of supposed idiosyncrasy to minute doses of cocain. X-ray treatment of the thyroid gland is of definite value.



FIG. 11.—Cretin, male, aged twenty-one years. (Bourneville and Bricon.)

Diminished Thyroid Secretion.—*Hypothyroidism* or *myxedema*, the acquired form in adults, and cretinism, the congenital form or acquired in infancy, is due to thyroid insufficiency and presents a picture quite in contrast to hyperthyroidism. Instead of a tendency to fever there is subnormal temperature and cool skin. Instead of mental



FIG. 12.—Simple goiter.

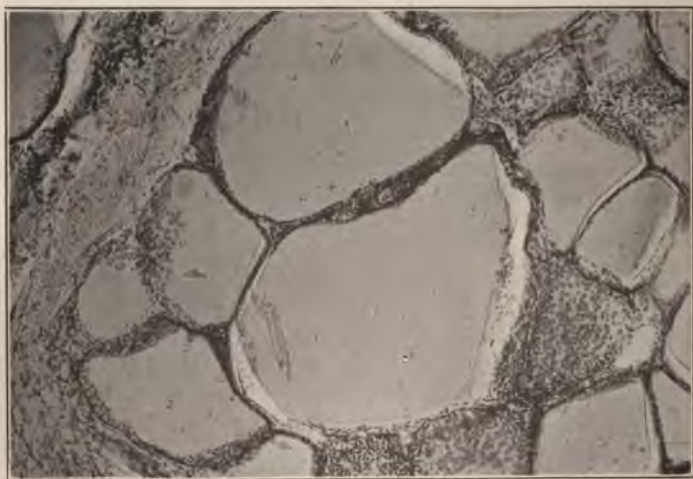


FIG. 13.—Colloid goiter. The glandular acini are filled with colloid material.

excitation there is mental sluggishness. The pulse is slow, weight is increased and most characteristic is the deposit of mucoid or myxomatous tissue subcutaneously giving the appearance of edema, hence the term myxedema. The tissues will not pit, however, on pressure. Myxedema usually comes on in women about middle life, due to atrophic changes in the thyroid gland. Sometimes the hypersecretion of earlier life "burns itself out" over a period of years and finally presents the picture of hyposecretion. Complete removal of the thyroid gland surgically also causes myxedema. Cretinism (Fig. 11), due to congenital absence of thyroid or its atrophy following some infection presents an extraordinary stunting of growth and mental development and the characteristic large, bloated face, thick lips, large, protruding tongue and general idiotic expression. Dentition is delayed and the teeth which appear decay early. The cases may reach adult age and retain the fat, chubby appearance of infants. Thyroid extract, obtained from animals, administered by mouth, is specific for hypothyroidism. The metabolism is entirely changed in a few weeks' time, but thyroid must be taken at intervals throughout life.

Pituitary Gland Disturbances.—The functions of the pituitary gland are not very well known, but there is now a great deal of evidence to indicate that it exerts a profound influence over bony growth. It has been called the proportion regulator of the skeleton. It is also involved in the process of puberty and adolescence. The extract of the gland is now used in a variety of ways in medical practice under the name of pituitrin. It stimulates contraction of unstriated muscle, especially of the uterus, and is used extensively by obstetricians to regulate uterine contractions and to control hemorrhage. Used hypodermically the action is prompt, powerful and dependable. The muscle of the intestinal and arterial walls is also affected. One might expect, therefore, that a condition of pituitary hypersecretion in life would induce bony overgrowth and sexual precocity, and that hyposecretion would result in retarded development. Clinically, these two types occur in the following diseases:

Increased Pituitary Secretion.—*Acromegaly* (literally large extremities) is a chronic disease, characterized by a slow

overgrowth of the bones of the extremities and face. There is a hypertrophy of the soft tissues as well. The hands are enlarged so that the patient is compelled to wear gloves two or three full sizes larger than his normal before the onset of the disease. The hand is broad and spade-like in shape. The superior and inferior maxillary bones are greatly enlarged, although the latter is more affected, so that it projects beyond the upper jaw (Fig. 14). The alveolar processes are widened and the teeth separated. This spacing of the teeth is an important and early sign of the



FIG. 14.—Typical case of acromegaly. (Hare.)

disease. The tongue is in some cases greatly enlarged. The skin of the face is thick and heavy. The voice may become coarse. Women may develop a deep, male voice. Menstruation may be disturbed early. The disease is more common among women, usually beginning at about twenty-five or thirty years of age. Eye symptoms are frequent, due to the close relation of the pituitary body to the optic tract. If the lesion is located at the optic chiasm it gives rise to the curious and localizing symptom of bitemporal hemianopia or blindness in the outer half of each retina.

In spite of this marked disturbance of growth, the general health and resistance of these patients often remain unimpaired for many years. Hyperpituitarism in childhood, of which a goodly number of cases are now on record, results in a variety of developmental freaks characterized especially by the maturing of the genital organs very early while the general bodily development is that of a young child.

Diminished Pituitary Secretion.—*Dystrophia adiposogenitalis*, or *Froehlich's syndrome*, represents the opposite condition of hypopituitarism. The genital organs are poorly developed; the general nutrition is usually subnormal with an excessive deposition of fat, sometimes giving certain female characteristics in men. Certain types of hermaphroditism are of this nature. There are sometimes curious mixtures of these opposite types described under the name of dyspituitarism.

Adrenal Gland Disturbances.—The adrenal gland is another small but vital organ, whose internal secretion constantly exerts a profound influence on bodily functions. The gland consists of a cortical and medullary portion, the latter being in very intimate relation with the sympathetic nervous system. The nervous connections of all the glands of internal secretion would suggest that the metabolic derangements that arise from nervous stress and strain, really result from changes in the internal secretions, which if abnormal act as toxins, not so unlike the etiological factors of disease previously considered. Probably the infinite variety of individual peculiarities of temperament and personality rest in part at least on the resultant of the interacting secretions. Adrenalin is perhaps the best known of these substances. It can be made synthetically as well as prepared from the gland. It produces an extreme vasoconstriction resulting in marked anemia on local application and in tremendous elevation of blood-pressure on intravenous administration. By analogy we should have two opposite conditions—one of hypersecretion with high blood-pressure, the other of hyposecretion with low blood-pressure. High blood-pressure conditions are frequent but not in association with primary disease of the adrenals. Cardiovascular renal degenerations form the pathological basis for high blood-

pressure with its resultant train of accidents such as apoplexy and heart failure. The precise mechanism by which high blood-pressure is produced is not known. The adrenal may play a rôle. There are cases of arterial hypertonus in fairly young people in whom there is little or no degeneration in the cardiovascular renal system. These may be due to a hyperadrenalinemia, although this has not been satisfactorily shown experimentally.

Diminished Adrenal Secretion.—*Addison's disease* presents a symptom-complex, which has been definitely associated with destructive lesions in the adrenal glands, thus representing adrenal hyposecretion. The most striking feature is the extreme weakness or asthenia, which is especially marked in the muscular and cardiovascular systems. The blood-pressure is very low, probably lower than in any other chronic disease. Ambulatory cases may have a systolic blood-pressure of 75 and diastolic of 55. The disease usually develops early in adult life. Pigmentation of the skin and mucous membranes from a bronze to black color is also an important symptom. It may begin in the skin as a deepening of the color in parts normally pigmented and extend to a diffuse melanosis. The oral mucosa may show blotches of quite dark pigment, sometimes more marked on the gums. Gastro-intestinal disturbances with nausea and vomiting occur at intervals. The disease tends to progress slowly but steadily to a fatal issue. The adrenal lesion is usually tuberculosis, most commonly secondary to a chronic or latent pulmonary tuberculosis. Treatment by adrenalin is disappointing. Some cases seem to improve, but never with the definiteness of thyroid extract in myxedema.

In connection with the other endocrine glands our knowledge is much less certain. If the sexual glands are removed before the age of puberty the secondary characteristics of sex do not develop. The glands are obviously closely related to the pituitary. The thymus and pineal glands have shown changes with disease of the thyroid and pituitary. In short, all the endocrine glands form a closely interrelated system, which exerts a very complex regulating influence on all the body functions.

CHAPTER VII.

RELATION OF ETIOLOGY TO PATHOLOGICAL PROCESSES.

IN the further development of the principles of pathology we may now turn from the viewpoint of etiology to that of the pathological processes themselves. Obviously the two cannot be entirely separated, since the cause, as, for instance, a specific germ, may be part of the pathological picture. Disturbances of function (pathological physiology) may be considered at the same time as the structural changes (morbid anatomy). It is the former which produces the symptoms of disease. The pathological processes may be considered under the following general headings:

1. Circulatory disturbances.
2. Pigmentation.
3. Degenerations and necrosis.
4. Inflammations.
5. Special infections.
6. Infectious granulomata.
7. Tumors.

CIRCULATORY DISTURBANCES.

The circulation directly affects and is part of all the tissues of the body. Therefore its disturbances are in the field of general pathology, not in the special pathology of one system or organ. The simplest conception of the circulatory system is that of a closed system of tubes with a central pumping station, the heart which is but a special development of the musculature of the system of tubes and continuous with it. Valves are simply mechanical necessities in the hydraulics of the circulation. The pumping power is

the automatic contraction of the heart muscle. Elasticity in the system, to meet varying circulatory needs in different places at different times, is provided by the vital vasomotor mechanism, which is under nervous control. Defects in the system, whether in the motor power, the valves, the vascular tubing, the vasomotor control or in abnormalities of the contained blood, will lead to changes in the tissues.

Results of Failing Circulation.—Cardiac insufficiency is a general term for inadequate circulation due either to weakness of the heart muscles or to defects in the valves. Stagnation of the blood must result back of the chamber, which fails to propel its portion of blood normally. If this is the left ventricle there is congestion in the left auricle and lungs. If this extends back to the right ventricle there is stasis in the right auricle and systemic veins, damming the blood back in all the organs, such as the liver, kidneys and lower extremities. These parts become swollen from congestion, lymph exudes causing edema or dropsy, as will shortly be described. Albumin and blood in the urine may result from congestion of the kidney. Fluid may be poured out into the peritoneal and pleural cavity. Shortness of breath (dyspnea) and cyanosis are early symptoms from involvement of the lungs and insufficient oxygenation of the blood. In the last analysis this circulatory failure is due to incompetency of the myocardium. So long as the heart compensates for valvular leakages or obstructions as it does by enlarging just as skeletal muscles do when constantly doing extra work the circulation proceeds normally. If the heart muscle or the myocardium is weak from anemia, poisonings or any of the degenerations later to be considered, the circulation stagnates accordingly even with perfect valve function. This condition inevitably comes in old age sooner or later if the individual escapes death from other causes. It may come in youth when the heart is diseased. The picture of circulatory failure, also called decompensation or broken compensation is the same whatever form of heart disease has caused it. This picture the dentist may learn to recognize without going into the differential diagnosis of valvular and other heart diseases. In fact, even for the physician the most important

consideration and the best criterion of the patient's endurance or preparedness for anesthesia and operation is just this circulatory competency and reserve. The mild, early stages of myocardial insufficiency may give rise to a great variety of functional disturbances and symptoms. Shortness of breath, cyanosis and tendency to rapid pulse independent of emotional excitement may be taken as definite indications that the patient is nearing the "breaking point" or cardiac decompensation. Such patients may die suddenly under anesthesia or shock. Well-compensated valvular heart cases, especially in young people, usually stand anesthesia very well.

General Nature of Heart Disease.—Heart diseases in a very broad way are of two kinds:

1. *Acute infections and inflammations in the first half of life.*
2. *Chronic infections and degenerations in the second half of life.*

The first group in the majority of cases are due to inflammatory rheumatism, the infection gaining entrance, as a rule, through the tonsils. All of the infectious diseases, such as pneumonia, scarlet fever, influenza, erysipelas and occasionally abscessed teeth may set up these acute inflammations in the heart, usually beginning on the mitral valve and extending on the endocardium. This is endocarditis. Inflammation, vegetations and cicatricial contraction of the valve leaflets lead to leakage (insufficiency) or narrowing and obstruction (stenosis). These defects obviously make the heart work at a mechanical disadvantage, for which it compensates by dilatation of its chambers and thickening of its muscular wall. The second group of heart diseases are due to chronic infections, especially syphilis, chronic intoxications, such as alcohol and lead, and metabolic diseases, and to the simple wear and tear of time which leads to a process of hardening (sclerosis) and fibrous tissue replacement of muscle in the heart and arteries. The arteriosclerosis leads to secondary changes in the other organs, especially the kidney (Bright's disease) which forms a vicious circle reacting on the heart, especially by way of elevated blood-pressure. These conditions involve the heart muscle and the aortic valves and wall. Syphilis particularly attacks the aorta

and its valves, leading to aortic insufficiency and dilatation and loss of elasticity. This gives a general view of the large subject of heart disease. The important thing as stated before is the functional integrity of the heart muscle.

Nature of Vascular Disorders.—The peripheral vascular disturbances may now be taken up. The vasomotor nervous mechanism is occasionally subject to curious perversions, the most extreme of which is spasm and constriction of the arterioles to the point of actually shutting off the circulation. This is the rather rare condition known as Raynaud's disease. It leads to pallor, pain and finally gangrene of the tips of the fingers or toes and rarely of the nose and ears. Transient *vascular spasm* is frequent in older people with arteriosclerosis, especially with high blood-pressure. If this occurs in muscles, intermittent cramps are produced, especially on use of the muscles. If it occurs in the brain there is temporary loss of function of the part deprived of its blood supply. If this is the motor area there is paralysis of one side of the body. If it is the speech center there is aphasia or inability to speak. If it is the higher centers there is loss of consciousness. These symptoms pass off with the relaxation of the contracted vessels and the return of blood to the affected parts. While the condition lasts it may be indistinguishable from that due to destruction of brain tissue, as from hemorrhage from a ruptured cerebral artery (apoplexy). These transient and sometimes quite persistent vascular spasms in old people are of practical importance to the dentist, because they may be induced by infections about the teeth or elsewhere and to poisons, such as alcohol, tobacco, drugs and by auto-intoxication.

Vasomotor Reactions to Certain Substances.—Vasomotor disturbances sometimes lead to localized swellings in the skin or mucous membranes known as angioneurotic edema. This may come on in a few minutes and after a while disappear within a few minutes just as blushing, a vasomotor phenomenon, may come and go. *Angioneurotic edema* frequently attacks the lips and eyelids, causing disfiguring swellings like bee stings. Urticaria or hives may be closely related. Similar phenomena may be on the basis of anaphylaxis or

sensitization to certain food substances, as strawberries, in susceptible individuals, egg albumen, at times in infants or to inhaled particles, as the pollen of plants, in hay fever.

CONGESTION.

Local Circulatory Lesions.—A more detailed consideration of circulatory disturbances may be begun with hyperemia, which, as the word indicates, is simply an excess of blood.

1. *Local Hyperemia* may be *physiological*, the blood being distributed under the control of vasomotor system according to physiological needs. For example there is engorgement of the splanchnic vessels at the height of digestion. There is also an increased amount of blood in the brain during mental activity and relatively less during sleep. The same applies to muscles and glands under the stimulus of active functioning.

2. *Active Hyperemia* is an excess of blood in a part due to dilatation of arteries. There is an increased flow to the part. This may be due to nervous influence or to the toxic action of drugs or other substances, but usually represents the first stage of inflammation. The hyperemic organ or area is redder than normal in color, the temperature is elevated and there is slight swelling due to an actual increase of blood in the part and transudation of serum into the tissues.

3. *Passive Hyperemia* or congestion, is due to obstruction to the outflow of blood from the vein of a part. This may be due to a simple pressure on the vein such as by tumors or circutricular bands or to clotting of the blood within the vein. The main cause of passive congestion, however, is myocardial insufficiency as described above, with stasis in the systemic veins. The liver illustrates passive congestion very typically. The central veins of the lobules are dilated so as to be just visible to the naked eye, giving a dotted appearance of the cut surface of the liver similar to that of a nutmeg. Hence the term nutmeg liver is used as descriptive of passive congestion of the liver. The whole organ is so enlarged that there is painful tension on the capsule of Glisson. The

passively congested organ is bluish and cyanotic from engorgement with venous blood. There may also be a transudation of serum into the tissues producing edema in chronic passive congestion. Secondary degenerations result in the cells on account of the impaired nutrition, such as fatty degeneration in the nutmeg liver. There may also be marked overgrowth of connective tissue and deposition of pigment due to broken-down blood corpuscles. The latter condition is called *brown induration*. Passive congestion apparently exercises an inhibiting influence on bacterial growth due to the excess of venous blood, so that secondary infection is infrequent even though the nutrition of the tissues is impaired. Advantage is taken of this in the treatment of certain infections by inducing passive hyperemia mechanically as by a pressure bandage or suction cup. This is known as Bier's hyperemia. It may be applied to abscesses and sinuses of the jaws.

4. *Hypostatic Congestion* is due to simple gravitation of the blood into the dependent parts. This occurs in the aged when they are kept flat in bed for undue periods of time. The dentist should be familiar with this danger in old or feeble patients. If there is severe reaction following extraction of a tooth, especially in the presence of infection, so that the patient must be put at rest, it is important that he be shifted from side to side or to a semi-sitting posture every few hours, otherwise hypostatic congestion results, which may easily be converted into a fatal pneumonia.

5. Postmortem congestion is a condition of interest mainly to those doing autopsies in which there is a similar stasis in the dependent parts, the location depending upon the position of the body at death.

General Blood Changes.—Hyperemia may also be general under rare conditions. It is then known as polycythemia, an excess of *red blood cells*, which normally number 5,000,000 per cubic millimeter. The increase per unit of volume may be due simply to concentration, as by the draining away of fluid from the blood in severe dysentery. There may also be an actual increase due to compensatory response on the part of the blood-forming bone-marrow, when the body

requires greater oxygen-carrying power in the blood. When the partial pressure of oxygen is low, as at high altitudes, or in a balloon ascent the red blood count may increase from 5,000,000 to as high as 8,000,000. A similar mobilization of red cells has been observed in carbon-monoxide poisoning, which interferes with the oxygen-carrying function of the hemoglobin. Conditions associated with cyanosis, such as chronic acetanilide poisoning and emphysema of the lungs, may show a polycythemia. Finally there are rare cases of polycythemia with cyanosis and enlarged spleen without any discoverable cause. Symptoms suggestive of imperfect oxygenation are, however, usually present such as vertigo and weakness and postmortem there is an abundance of red bone-marrow.

An excess of *white blood corpuscles* over the normal of 7500 per cubic millimeter is called *leukocytosis*. This occurs as a defensive response to many infections and intoxications, such as abscesses, throat infections and pneumonia. A leukocytosis of 30,000 in pneumonia is frequent. The pus cells of a local suppuration are degenerated leukocytes. This will be considered in detail under the heading of inflammation.

HEMORRHAGE.

Forms of Hemorrhage.—Hemorrhage is the escape of the blood constituents from the closed system of tubes composing the circulatory tree. If this is by gross rupture of a blood-vessel it is termed *rhexis*. If it is by microscopic oozing of blood cells through the capillary walls it is *diapedesis*. Under normal conditions a certain number of white corpuscles due to their ameboid movement find their way through endothelial walls of the capillaries and are carried in the lymph-vessels. Under abnormal conditions such as increased blood-pressure the red corpuscles also pass through the vessel wall. Localized infection may lead to increased permeability of the capillary endothelium and result in small punctate hemorrhages known as *petechiæ*. These appear in the skin as tiny red spots and are sometimes symptomatic of general infections and intoxications. *Ecchymosis* is a larger localized

effusion of blood into the tissues. Hematoma (blood tumor) is a collection of extravasated blood forming a circumscribed swelling or tumor. The blood may be clotted and very firm in consistency so that clinically it must be differentiated from real tumors especially if the source of hemorrhage is not apparent. Hematoma of the scalp following contusion is sometimes deceptive—also in the neck or floor of the mouth following fracture of the jaw. There may also be spontaneous hemorrhage within malignant tumors in the neck. As a rule hematoma may be left to absorb. It may, however, be secondarily infected and require drainage as an ordinary abscess.

Causes of Hemorrhage.—The causes of hemorrhage may be considered under the following general headings:

1. *Simple trauma* may cause rhexis by directly opening a vessel, or diapedesis, by contusion, which weakens the bloodvessel wall and increases permeability.

2. *Disease of the bloodvessel* wall due to infections, intoxications or to the simple degeneration of age. There may also be erosion of the bloodvessel wall from the outside such as by the pressure of a tumor or necrosis in the extravascular tissue.

3. *Abnormalities of the blood itself* such as faulty coagulating power, anemias, or leukemias in which there is an abnormal increase in the white blood corpuscles.

4. *Increase of blood-pressure* may directly rupture a bloodvessel as, for instance, in the brain in apoplexy. There may be an increase of venous blood-pressure by mechanical obstruction to the return circulation resulting in hemorrhage as, for instance, in varicose veins of the leg.

5. *Neuropathic hemorrhage* is a term which has been applied to certain ill-defined forms of bleeding, which sometimes come under great nervous excitement. The process is probably related to the above-mentioned condition of angioneurotic edema.

6. *Hemophilia* (love of blood) or the hemorrhagic diathesis is a form of constitutional tendency to bleeding in apparently normal individuals. This is the congenital or hereditary form of hemophilia. The subjects of this condition are

popularly called bleeders. From early childhood they show a tendency to persistent bleeding from slight cuts or injuries.

Hemophilic Joints.—There is often recurrent hemorrhage into the joints especially the knees, causing acute inflammation, which may require rest in bed for weeks. There is a bloody effusion into the joints and at times discoloration of the overlying skin. The term hemophilic joint is applied to this condition. Severe bleeding following the extraction of a tooth, even fatal hemorrhage has occurred in these bleeders. Dentists should pay due attention to a history of repeated hemorrhages following slight injuries. Congenital hemophilia is a hereditary characteristic in certain families and is transmitted by the female members and inherited by the male members. This law has been established with very rare exceptions in many families through a number of generations. True bleeders then are practically always males. Hemophilia in female patients is suspected to be secondary to some other bodily condition. The exact nature of the defect in hemophilia is not known. The coagulation time is prolonged in certain cases and normal in others. In the latter there may be an abnormal frangibility of the capillary walls. In some cases there are probably substances lacking in the blood serum necessary in the complex chemical process of blood coagulation. Even if the coagulation occurs in the proper time the clot may not have normal firmness or adhering properties. This is the basis of treatment by serum injections and calcium salts with the idea of supplying the missing elements.

Acquired Hemophilia.—There is an acquired form of hemophilia, which is due to infections or metabolic diseases. Scurvy as previously described with its bleeding from the gums and into the skin is an example of acquired hemophilia based upon a metabolic disorder the exact nature of which is unknown. Rheumatic infection and septicemia may cause severe hemorrhages. In fact all severe forms of infectious diseases may be associated with hemorrhage in their lesions. The dark color of the changed blood pigment has given rise to the popular term "black" such as "black small-pox," "black diphtheria" or "black measles."

ANEMIA.

Forms of Anemia.—Anemia is a lack of blood, either a reduction in the number of red cells (oligocythemia) or in the amount of hemoglobin (oligochromemia). As in hyperemia this may be local or general.

Local anemia results from a cessation of the arterial inflow to a part. This may be due to: (1) Pressure from outside the artery, as by a tumor, a tourniquet or even inflammatory swelling. (2) Obstruction within the artery, such as coagulation of the blood (thrombosis) or the presence of a foreign body (embolism) or an intravascular growth or extreme thickening of the arterial walls, as in senile arteriosclerosis. (3) Vasomotor constriction, which may be slight or extreme as described under Raynaud's disease and vascular spasm. Local anemia leads first to impairment of function and later to loss of function, fatty and other degenerations in the affected parts and finally to necrosis or gangrene.

General Anemia (less than 5,000,000 red cells per cubic millimeter or less than 90 to 100 per cent. of hemoglobin) is usually divided into two classes, primary and secondary. The latter is due to some other condition, such as chronic infection, intoxication or hemorrhage. Primary anemia is a severe form in which no underlying cause can be discovered. Some cases are considered primary at first and later prove to be secondary to other conditions such as hemolytic streptococcus infections at the roots of dead teeth and at other foci, certain parasites especially the fish tapeworm (*bothriocephalus latus*) malignant tumors or slow repeated hemorrhages. There are two forms, however, pernicious anemia and chlorosis, which have a rather characteristic blood picture and in which there is no known etiology.

The Primary Anemias.—*Pernicious and Chlorotic.*—*Pernicious Anemia* presents certain characteristic clinical features. The patient has a curious lemon yellow tint and is usually well nourished, unlike most of the severe secondary anemias. The loss of strength and endurance is out of proportion at least to the loss of weight. The symptoms of any severe anemia are present namely, dizziness, headache,

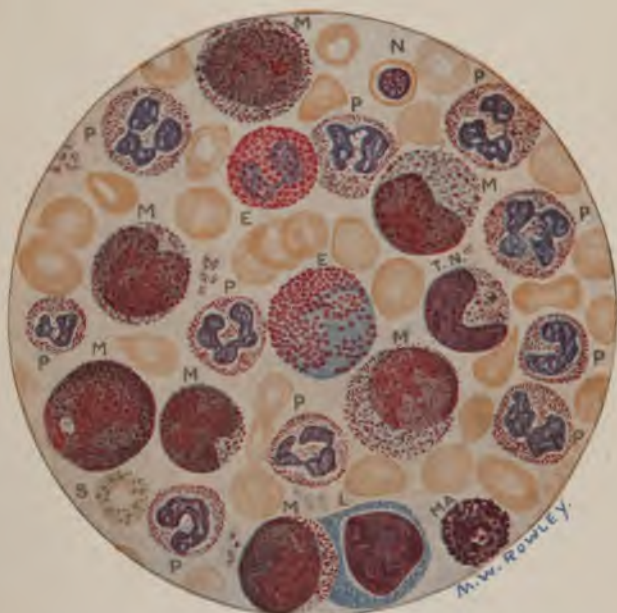
breathlessness, ringing in the ears, faintness and palpitation. There may be marked remissions in the course of the disease especially under arsenic treatment, but a fatal recurrence usually comes within a few years. The blood smear shows many fragmented and irregular red cells (poikilocytes) but with good hemoglobin content, as though there were some destructive agent at work. The red blood count may be as low as 500,000. The hemoglobin is much less reduced, so that the color index (which is the ratio of hemoglobin percentage of normal to the cell percentage of normal) is greater than one. This is usually less than one in the secondary anemias. There are also nucleated red blood corpuscles in the blood and evidences of hyperactivity in the bone-marrow. This of course is regarded as an effort on the part of nature to replace the destroyed cells. There are rare cases in which this regenerative power is lost and the bone-marrow becomes fatty and atrophic. This is known as aplastic (without growth) anemia. Blood pigment liberated by the hemolysis is deposited in the liver and spleen or excreted. The condition is usually associated with chronic gastro-intestinal disorders and is also related in certain cases to pregnancy. Secondary degenerations in the internal organs especially the liver and heart muscle in the later stages of the disease are the rule. Changes in the nervous system also occur, at times leading to disability similar to that of locomotor ataxia. Certain stages of the disease may show prolonged fever, so that infection is suggested at least as an etiological agent. From the dental standpoint it may be said that the teeth are usually the first site of focal infection sought for, but there are many disappointments after the removal of infected teeth. However, it is often not done radically enough. Dead teeth which appear normal or nearly normal in the x-ray film are usually left in the mouth, although it is known that there is infection at the root as a rule. There is even some evidence that it is just this condition without marked local reaction or abscess formation, which permits of the escape of bacteria into the blood stream. The abscess wall is a defense reaction. It is also possible that if the blood-forming tissues are injured too severely or for too

long a time, their power of regeneration may be destroyed, so that the removal of the original cause does not cure the disease. Therefore the dental origin of many cases of primary anemia cannot easily be excluded.

Dental Considerations.—In extractions in these cases, the dentist should be prepared to control hemorrhage, since severe anemias at times cause troublesome and prolonged bleeding. The presence of skin petechiæ or the history of hemorrhages from the nose or from the bowel or bladder would serve as an indication for caution. Serum injection is the best therapeutic measure in addition to local hemostasis. These considerations emphasize the importance of prophylaxis against root infection in the management of dead teeth.

Chlorosis differs radically from pernicious anemia in that it runs a favorable course and is a reduction in hemoglobin much in excess of the reduction in the number of red cells. The red cells are well formed and show large central pale areas. The color index is less than one. In severe degrees of chlorosis, there are a few nucleated red cells (normoblasts). The disease is found almost entirely in girls or young women, especially when living under unhygienic conditions. Irish immigrant girls have been peculiarly subject to it. A tuberculous heredity seems to be a factor in some cases. A lack of development (hypoplasia) of the circulatory and reproductive organs has frequently been observed. Gastrointestinal and menstrual disorders are frequent but are probably the result rather than the cause of the anemia. The exact etiology is not known. Chlorosis is therefore classified as a primary anemia. It may really depend upon a disturbance of the internal secretions occurring as part of the process of puberty and adolescence. Iron is a specific cure for chlorosis, but the anemia may recur during early adult life. Unlike anemias secondary to tuberculosis or other infections, chlorosis as well as pernicious anemia does not cause marked emaciation. Subcutaneous fat is in contrast to the severity of the anemia. The name chlorosis (green sickness) refers to the peculiar pallor sometimes of a slight greenish tint seen in these cases.

PLATE III



Myelogenic Leukemia. Copied from an Actual Field.
(Cabot.)

P, polynuclear neutrophilic leukocytes; *M*, neutrophilic myelocytes;
T.N., transitional neutrophile; *MA*, mast cell; *L*, "marrow lymphocyte";
E, E, polynuclear eosinophiles; *S*, "stippled" erythrocyte; *N*, normoblast.

Dental Consideration.—The severe degree of the primary anemias necessarily results in marked lowering of the bodily resistance to infections and shock. Dilatation of the heart and myocardial insufficiency are frequent. In chlorosis, dental work except of an emergency or temporary character should be deferred for a month or two, so that the blood condition and general resistance can be improved. The same applies to the latter months of pregnancy. Temporary fillings may be used to check the progress of caries and later when the calcium content of the body is normal and the softened condition of the teeth is overcome, permanent fillings may be used more successfully.

OTHER BLOOD DISEASES.

Leukemia may be considered briefly in connection with primary blood disorders. Leukemia (white blood) is an enormous increase of the white blood corpuscles—300,000 to 500,000 per cubic millimeter. Its etiology is unknown. In many respects it acts like a malignant tumor of the blood-forming tissues, in other respects like a chronic infection. There are two forms—the splenomyelogenous and the lymphatic. The former is characterized, as the term indicates, by an overgrowth of the bone-marrow and spleen and a flooding of the blood stream with cells known as myelocytes, destined to form leukocytes (Plate III). The spleen may enlarge quite down to the pelvis. Lymphatic leukemia is characterized by an overgrowth of the lymph glands all over the body and a flooding of the blood stream with lymphocytes. Leukemia is a rather rare disease and affects the body much like a severe anemia. It may be essentially a manifestation of chronic sepsis. There is some evidence that certain leukemias are infections arising in the oral cavity.

THE RELATION OF BLOOD DISEASES TO DENTISTRY.

These primary blood diseases, pernicious anemia, chlorosis, leukemia and congenital hemophilia, together with certain less well-known intermediate or related conditions have a direct

bearing on pathological processes. For example, intravascular coagulation about to be considered under thrombosis and embolism may be due to an abnormality of the blood as a tissue. So long as the intimal lining of a bloodvessel is intact normal blood remains fluid for a long period even when not circulating. Since all the organs including the teeth are directly dependent on their circulation for life as well as for all processes of healing and repair, the condition of the blood itself as a tissue is fundamental. All local conditions whether in the dental sphere or in the field of any other specialty such as the eye are of secondary importance in a patient with a primary blood dyscrasia. Mechanical perfection in dental work would be of no avail in a patient with leukemia.

THE PRINCIPLES OF BLOOD TRANSFUSION.

In connection with the subjects of hemorrhage and anemia the principles underlying blood transfusion may be considered. Obviously when there is a marked loss of blood it would be very desirable to replace the loss with blood from another individual. This idea dates back to the fifteenth century. However, attempts at transfusion were unsuccessful in those early days. The discovery of the circulation of the blood by Harvey was not made until 1628 and it would be difficult to imagine a successful transfusion without this fundamental knowledge. It was only with the later development of physiology and surgery that blood transfusion was actually carried out. The most marked progress has been made in the last fifteen years. The first transfusions were made by suture of the artery of the donor to the vein of the recipient. This was a very difficult technical procedure and the coagulation of the blood was a constant annoyance. Several types of cannulas were used for direct transfusion from artery to vein. The intimal lining of the two vessels being brought together. Later paraffin-lined tubes were used in which blood could be kept for a few minutes without coagulating. The blood was then taken from the vein of the donor and at once transferred into the vein of the recipient. Latterly, however, transfusion by the use of anticoagulants has largely replaced previous

methods. Sodium citrate of a concentration of 0.2 per cent. is harmless and very efficient in preventing blood coagulation for several days. Blood may then be taken from the vein of the donor received into a 2 per cent. solution of sodium citrate and ten times the quantity of blood drawn as of the citrate solution so that the concentration of the citrate in blood is 0.2 per cent. It may then be given at leisure as a simple intravenous injection into the vein of the recipient. Technical difficulties in connection with the coagulation of the blood are eliminated by this method. It is also advantageous because it does not require the recipient and donor to be brought together.

The more frequent use of transfusion soon brought out the fact that all bloods are not compatible with each other. In about 4 per cent. of cases severe reactions followed shortly after transfusion, an occasional one ending fatally. This led to the method of testing blood in advance by incubating blood serum of the donor with the washed red blood corpuscles of the recipient and the red blood corpuscles of the donor with the serum of the recipient. In incompatible blood there is either agglutination or hemolysis of red cells. This may be recognized by a gross suspension of cells or in a hanging drop under the microscope. It is found by these tests that all blood samples fall in one of four groups and that reactions following transfusion do not occur when recipient and donor belong to the same group. Blood relatives are more apt to belong to the same group. Except in the greatest emergencies blood tests should be carried out before transfusion is undertaken. The dentist working on cases of severe hemophilia may encounter uncontrollable hemorrhages from extraction of teeth. In these cases transfusion might prove to be a life-saving measure.

CHAPTER VIII.

CIRCULATORY DISTURBANCES (CONTINUED).

THROMBOSIS AND EMBOLISM.

Thrombosis is the coagulation of blood within the blood-vessels or heart. It is due to changes in the vessel walls or in the blood itself, resulting in the liberation of thromboplastic substances, which start the process of coagulation—prothrombin to thrombin, which with the fibrinogen of the blood plasma forms the fibrin of a clot or coagulum. The experiment of the “living test-tube” shows that blood may be kept for days without coagulating in an excised vein if the ends are gently closed without injuring the intima in contact with the blood. The addition of any cellular or tissue extract promptly induces coagulation.

Causes of Thrombosis.—The most common cause of thrombosis is *injury* or *infection* of the vascular wall. It is nature's method of hemostasis in wounds or disease. Surgical ligation of vessels is followed by thrombosis and the clot or thrombus occludes the vessel after the ligature is absorbed. Infection of the endothelial lining of a vessel, especially of a vein, (phlebitis) leading to coagulation (thrombophlebitis) frequently complicates the infectious diseases such as typhoid fever, pneumonia or a septic state arising from infection in the mouth or neck. In the latter case bacteria are frequently carried through deep veins, such as the deep facial vein to the venous sinuses within the skull, resulting in sinus thrombosis, especially of the cavernous sinus. Similarly lateral sinus thrombosis results by infection from the middle ear or mastoid. Such extension of infection is determined largely by the state of the general bodily resistance. Old age and chronic disease are strong predisposing factors. The tearing open of tissue spaces, such as occurs in extraction of a tooth

favors the spread of infection. An alveolar abscess, therefore, especially in an old person, should be incised and drained until the acute infection subsides before the tooth is extracted. Primary extraction has resulted in sinus thrombosis and septicemia. Marked slowing of the blood current favors thrombosis. For this reason the veins are more affected than arteries. General circulatory failure or chronic asthenic diseases are at times complicated by thrombosis. This is known as marasmic or *marantic thrombosis*. In many of these cases, however, there are secondary factors especially low grade infection. Chronic lesions—sclerosis or other degeneration in the intima may serve as the starting point. At times thrombophlebitis especially of the left femoral vein follows aseptic operations. In some of these mild infection is present. In oral surgery this possibility can never be excluded. Finally primary *abnormalities of the blood* itself such as leukemia or hemolysis may cause thrombosis.

Results of Thrombosis.—When the process of coagulation starts the exact structures of the thrombus depends upon several factors, especially the rate of blood flow. If this is very sluggish, the thrombus is much like any ordinary blood clot, red blood cells in a network of fibrin. If the thrombus forms gradually at the side of a rapid blood stream, leukocytes predominate, the admixture of red cells varying at different times and thus forming a stratified structure. Secondary contraction, extrusion of red cells and hyaline and other changes result in the formation of yellow and white thrombi. Calcification may occur in them, producing the so-called vein stones or phleboliths. A variety of terms are used to describe various kinds of thrombi—*parietal* or *lateral* when attached to the wall of vessel, *occluding* or *obstructing* when filling the lumen. *Ball thrombi* are masses lying free, usually in the auricles of the heart. Similar *polypoid* forms may be attached by a small pedicle. A septic thrombus is one in which there is active infection. It may cause a localized abscess, but frequently is the starting-point of septicemia or pyemia. The “chicken fat” clot forms post mortem in the plasma after the red cells have settled out. *Organization* of a thrombus consists in a gradual vascularization of the mass,

the absorption of the dead elements and a replacement by living connective tissue. The organized thrombus is then living tissue instead of a foreign body. The ingrowth of new capillaries proceeds much as in granulation tissue. New

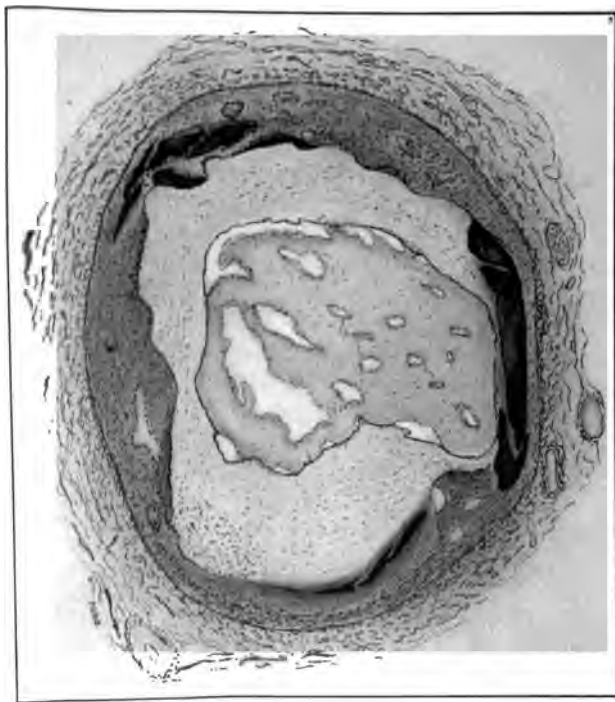


FIG. 15.—Tibial artery, sclerosed, with organized and canalized thrombi. The clear spaces represent what is now the lumen of the vessel. From a case of senile gangrene of the foot. (Oskar Klotz.)

channels are often formed entirely through the thrombus, so that the circulation is in part at least restored. This is called *canalization* of the thrombus (Figs. 15 and 16). It may be so extensive as to reduce the original thrombus to a few fibrous strands.

Causes of Embolism.—*Embolism* is the transportation of foreign bodies in the blood stream. Any such foreign body is called an embolus. This may consist of a variety of substances. A detached thrombus becomes an embolus. A broken off vegetation from a heart valve in endocarditis is perhaps the most common variety of embolus. Emboli may arise similarly from patches of atheroma in the aorta. Particles of fat from bone-marrow after fractures of bones find their way into the circulation. In wounds of the neck, air may be aspirated into the veins and act as an embolus. Air may also be injected through a hypodermic needle. In intramuscular injections of suspensions of insoluble drugs, it is important to determine by detaching the syringe or aspirating that the point of the needle is not in a vein. The same applies to paraffin injections to correct deformities about the face. Masses of cells, whether metastases from malignant tumors or giant cells from bone or parenchymal cells from a compressed or contused organ such as the liver, may cause embolism. Gas embolism may result from infection by gas-forming bacilli or in caisson disease following decompression. In the latter case the gas is the nitrogen of air reappearing in the blood upon the release of external pressure. Oxygen remains in combination with hemoglobin. Blood parasites such as malarial organisms and the pigment



FIG. 16.—Acute red thrombus of iliac vein. (McGill Medical Museum.)

of disintegrated red blood cells and the trypanosomes of African sleeping sickness may act as emboli. This list shows the wide application of the process of embolism in pathology.

INFARCTION.

The results of embolism and thrombosis are mainly due to obstruction of the circulation of the affected part. Embolism may cause thrombosis and thrombosis may cause embolism. Either may obstruct the circulation to a part and if the collateral circulation is not sufficient for its needs there result ultimately degeneration and necrosis.

This process is called *infarction* and the affected area an *infarct* (Fig. 17). The typical process is seen in connection with the so-called end-arteries which supply exclusively or nearly so a certain section of tissue. In the kidney, for instance, an infarct is a wedge-shaped or conical mass of degenerated tissue with the base toward the outside of the kidney and the apex at the occluded artery. There is some collateral circulation, however. The first stage of infarction is a swelling and enlargement with venous blood. This is

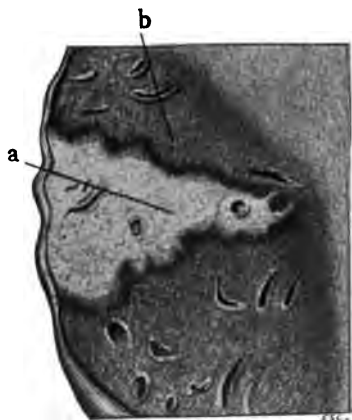


FIG. 17.—Section from white infarct of spleen: a, infarct; b, surrounding splenic tissue with zone of congestion surrounding infarct. (Adami and McCrae.)

the *hemorrhagic* or red *infarct*. Later the blood pigment is absorbed and granular, hyaline and other degenerations occur and an overgrowth of connective tissue. This is the *anemic* or *white infarct*. Finally a puckered cicatrix may be the only evidence of the old infarct. If the collateral circulation is quite good as in the lung the process may not go beyond the stage of congestion, which may completely resolve

and clear up. A few dead cells are readily carried away by the leukocytes. There may also be a process of organization or of calcification just as in a thrombus. An infected or so-called septic embolus may obviously start a suppurative process. A cellular embolus from a malignant growth gives origin to a metastatic tumor. In the brain, an infarct may undergo liquifaction and become encapsulated or "encysted" forming a brain cyst. In this way there is no cicatricial contraction or distortion of the parts. It is the brain's way of disposing of degenerated areas of various kinds.



FIG. 18.—Aortic endocarditis with vegetation (a). (Adami and McCrae.)

Results of Infarction.—The functional disturbances or clinical symptoms of infarction resulting from thrombosis or embolism depend entirely on the part affected. In the brain, the shutting off of the circulation to certain parts results in the same type of symptoms as were described under vascular spasm except that they are more permanent. A large cerebral embolus may cause sudden death or paralysis of one side of the body (hemiplegia) or of one extremity (monoplegia) or loss of speech (aphasia). Such a sudden development following fracture of a bone suggests at once fat embolism. If it occurs in a patient with valvular heart disease it is most probably due to a brushing off of a vegetation due to endocarditis into the blood stream (Fig. 18). If it occurs in a patient with a thrombophlebitis following some infection it is attributed to a detached thrombus. Abscesses in the mouth, throat or neck as stated before may cause septic thrombosis of the venous sinuses within the skull,

especially the cavernous sinus. This obstructs the ophthalmic veins in the orbit and produces bulging of the eyes (*exophthalmos*). Emboli originating in the veins pass into the right heart and to lungs causing pulmonary infarction. Small emboli, however, may pass through the capillaries of the lungs and lodge in the brain. If the foramen ovale is patent, they may pass directly through the left auricle and ventricle and out through the aorta (crossed or paradoxical embolism). *Pulmonary infarction* if extensive, such as occurs when a large clot from the femoral vein or vena cava plugs a primary trunk of the pulmonary artery, may be promptly fatal. Smaller infarcts with their congestion act somewhat like areas of pneumonia. There may be pain from involvement of the overlying pleura and bloody sputum. There is usually not much fever, however, because the process is not primarily an infection. Similarly infarction of the kidney causes bloody urine (*hematuria*). Embolism or thrombosis of the larger mesenteric vessels paralyzes the affected portion of the intestine causing intestinal obstruction and gangrene of the bowel. Infarction does not occur in the muscles or connective tissues because of the very free anastomosis of blood-vessels. Small emboli may cause only partial occlusion and only temporary symptoms.

TRANSUDATION.

Definition.—Transudation is the passage of fluid from the bloodvessels into the tissues with little or no admixture of cellular elements. This is distinguished from exudation which implies the pouring out of inflammatory cells and will be considered later. There is a normal amount of transudation, which is the origin of the lymph circulation. Excessive transudation leads to an accumulation of fluid in the interstices of the tissues, which become water-logged and pit on pressure. This is called *edema* or popularly “dropsy.” A diffuse generalized edema is called *anasarca*. An accumulation of transudate in the pleural cavity is “*hydrothorax*,” in the peritoneal cavity *ascites*, in the pericardial cavity *hydropericardium*.

The Nature of Transudation.—The exact nature of transudation is not very well understood. There are undoubtedly a

number of causes some of which are as follows: (1) *Increased venous pressure*, as in thrombosis or other obstruction in a vein or in broken compensation and general venous stasis as discussed under myocardial insufficiency. In the former there would be a local edema below the obstruction, in the latter a general edema or anasarca. (2) *Increased permeability* of the capillary endothelium of toxic origin. A great variety of exogenous and endogenous poisons may cause it. Arsenic poisoning it will be remembered produces as one of the earliest symptoms an edematous puffing about the eyes. Metabolic toxins in nephritis and in cachectic states and the toxins of infections and inflammations similarly cause edema. (3) *Osmosis* due to an abnormal concentration of salts, especially sodium chloride. An excessively salt diet sometimes leads to edema. A salt-free diet in cardiac edema aids in the elimination of fluid. (4) *Secretory function* of the capillary endothelium, probably also a toxic effect. (5) *Obstruction of the larger lymphatic channels*, such as the thoracic duct may cause edema. The filarial parasites obstruct the lymph channels in the groin and leg, resulting in a condition of edematous swelling and fibrous overgrowth known as elephantiasis. (6) *Nervous influences* may cause the so-called trophic edema or neuritic edema in acute neuritis and through the vasomotor system angioneurotic edema. (7) *Edema ex vacuo* is the simple mechanical drainage of lymph into a cavity. (8) Finally, the most recent explanation of the phenomena of transudation is on the basis of the *physical properties of colloid bodies* which are able to absorb excessive quantities of water when it is slightly acidulated. In the tissues many pathological conditions lead to an acidosis in response to which the colloid substances retain the excess fluid.

Inflammatory edema occurs readily and may cause a considerable degree of swelling in the mouth, face and neck due to the great vascularity, to the loose and lax connective tissue and to infection from the mouth. Edematous fluid accumulates in the loose tissue of the eyelids so that the eye may be quite closed, by extension of inflammation from an abscessed tooth. In deep infection in the neck, especially in children there may be edema of the larynx causing serious obstruction to breathing.

CHAPTER IX.

PIGMENTATION.

PIGMENTATION may be physiological under the stimulation of external agencies such as sunlight or of internal causes such as pregnancy. This is simply an increase in the amount of normal pigment. Pathological pigmentation may be considered briefly under four headings:

1. **Hematogenous** (Originating in the Blood).—This may be due to hemolysis in the circulating blood with deposition of pigment in the tissues as in pernicious anemia or malaria and many poisonings. Or it may result from chemical changes in local extravasations of blood as in a contusion of the face. These blood stains serve as telltale signs of old lesions such as fractures and ulcers. Hemosiderin is the yellow iron-containing pigment derived from the blood. Hematoidin is the reddish brown iron-free substance seen later in the course of blood absorption. The pigment granules occur either within the cells or in the intercellular spaces. Hemachromatosis is as the word indicates a generalized hematogenous pigmentation with deposits particularly in the liver and pancreas. Involvement of the latter is sometimes associated with diabetes. This with the skin pigmentation has been called bronzed diabetes.

2. **Hepatogenous** (Originating in the Liver).—The bile pigments bilirubin and biliverdin are very closely related chemically to hematoidin. In marked hemolysis, bilirubin cannot all be excreted and is absorbed causing jaundice, that is the yellowish staining of all the tissues. Jaundice, however, is usually due to obstruction of the bile ducts, by stone or inflammatory swelling, or to liver disease. The bile salts as well as the pigments are carried in the blood and produce characteristic symptoms in addition to the pigmen-

tion, especially lassitude, itching of the skin and slow pulse. Most of the secretions contain the bile pigment. The salivary, lachrymal and mammary secretions, however, are not usually colored. The sweat is a free channel of excretion as also the urine, which shows bile before the skin is stained. Complete obstruction of the bile ducts as by a malignant growth results in a deep olive green pigmentation of all the tissues of the body except possibly the brain substance.

Metabolic (Arising from Cellular Activity).—A great variety of pigments are formed in the chemical processes of the body. Many of them are derived indirectly from hemoglobin, others are products of proteid anabolism. Pigments are conspicuous by their color. By analogy it is apparent that unpigmented substances may similarly be produced in the body metabolism. This is the field of chemical pathology. General pigmentation results from disease of the medulla of the adrenal glands or of the closely related sympathetic ganglia (known as the chromaffin system) as was described under Addison's disease. Local pigmentation results from the chemical processes in certain tumors and in growths from pigment cells such as melanoma, arising from pigmented moles or the choroid of the eye. This will be considered under tumors. Certain degenerative processes are associated with the deposition of pigment granules such as "brown atrophy" of the heart muscle. Skin irritation may lead to an increase of pigment by prolonged pressure or friction of some mechanical device. X-ray treatments will cause pigmentation without burning. Pregnancy causes hyperpigmentation of the normally pigmented areas and often a blotchy discoloration of the skin especially of the forehead (chloasma uterinum). Occasionally there is a congenital pigmentation of the dentine of a tooth.

Extraneous.—Introduced from outside the body. Inhalation of dust in the various industries especially of coal, stone or iron dust leads to a deposit of colored particles in the submucosa or interstitial tissue of the lungs and in the regional lymph glands (Fig. 19). The lungs of coal workers are found at autopsy to be coal black. Stone dust is the most injurious. It leads to a fibrous overgrowth and loss of

elasticity of the lungs in addition to extensive deposits of lime or silica. The latter show very plainly in the x-ray plate. These patients become dyspneic and are predisposed to tuberculosis. The condition of deposits of foreign matter in the lungs is known as *pneumonokoniosis*. Coal dust in any ordinary amount is relatively harmless, providing it is not contaminated with infectious material. Certain drugs taken internally may also lead to pigmentation. Arsenic has been mentioned. Silver, after prolonged administration may be



FIG. 19.—Extraneous pigment. From section of an anthracotic lung to show fibrous areas enclosing deposits formed of fine coal-dust particles (high power).

deposited as an albuminate of silver in the intercellular spaces just under the epithelium of the skin or mucous membrane, producing a characteristic gray color (*argyria*). There may also be local pigmentation of tooth structures especially dentine by metals and dyes.

Albinism and Vitiligo.—Pigmentation is sometimes conspicuous by its absence either generally (albinism) or locally (vitiligo). Entire absence of pigment occurs in certain individuals congenitally. The hair is perfectly white. The iris without its curtain of pigment is transparent and pink as

in rabbits by reflected light from the vascular fundus of the eye. Albinos are therefore very sensitive to bright light. Localized loss of pigment (vitiligo or leukoderma) is closely related to nerve influence (Figs. 20 and 21). It may occur



FIG. 20.—Vitiligo.



FIG. 21.—Vitiligo.

symmetrically on the two sides of the body in the distribution of certain nerves. It is most frequent on the face, neck and hands. Hair in the involved areas is also colorless. It may last indefinitely without any associated disturbance of general health.

CHAPTER X.

ATROPHY, DEGENERATION AND NECROSIS.

ATROPHY.

Atrophy, plainly defined is a wasting of the tissues. More accurately it is a reduction in the size of the tissue elements or cells. This is specified in contrast to a reduction in the number of cells which is called *hypoplasia*. The two processes are frequently associated. *Aplasia* is the entire absence of cell growth as of the bone-marrow in aplastic anemia. In this connection several related terms may be defined. *Hypertrophy* is an overgrowth in the size of the cells, the opposite of atrophy. *Hyperplasia* is an increase in the number of cells, the opposite of hypoplasia. The two processes are also frequently associated as in the thyroid gland in goiter. Finally *metaplasia* is the change from one type of tissue to another type as connective tissue to bone.

Forms of Atrophy.—Atrophy results from a great variety of changes in the functional activity and nutrition of the tissues.

Physiological atrophy occurs in organs which are no longer needed in the organism such as the thymus after birth.

Senile atrophy is the retrogressive tissue change of old age. The circulatory system shows the effects of wear and tear early and as a result the nutrition of all the tissues suffers. Bones actually grow smaller and more fragile in old age. There is an atrophy of the cells and a failure to replace the normal absorption of lime salts. This is known as senile osteoporosis. The small delicate mandible of the edentulous jaw in old age is partly due to senile atrophy and partly due to atrophy of disuse from the absence of teeth. The neck of the femur may be so fragile in old age that it may be fractured by no greater violence than tripping on a carpet. Pyorrhea

alveolaris may prove to be primarily a process of atrophy of the alveolar process with a consequent recession and infection of the gum. There is an atrophy with osteoporosis and absorption of the alveolar process with advancing age, whether or not there is a secondary gingivitis. This is the basis of estimating age by the teeth.

Atrophy of impaired nutrition necessarily results from arterial disease or in starvation. From the latter spontaneous fractures of bones may occur as under recent war conditions. It is seen as an early change in an infarct.

Pressure atrophy is the compression and absorption of tissue, even bone, by prolonged pressure. Bone will gradually yield to continuous pressure even by a soft tissue such as a dilated aorta or aneurysm resting against the bodies of the vertebrae or the sternum. The basis of orthodontia is pressure atrophy. Continuous pressure of a tooth on one side of the alveolus leads to resorption of bone, while on the opposite side there is a secondary deposit of bone, so that after a long period of time, the changed or corrected position of the tooth is permanent.

Atrophy of disuse may be very marked. The circulation and nutrition are at low ebb in an organ that is not functioning, so that atrophy of disuse overlaps with atrophy of impaired nutrition. The muscles of a fractured arm after weeks of splinting are very wasted and weak. The muscles of mastication, especially the masseter, show atrophy after immobilization of the fractured jaw.

Neuropathic atrophy is due to loss of trophic influence through the nerves. In advanced neuritis there is a thinning and wasting of the skin of the affected region. After excision of the Gasserian ganglion with its motor root which supplies the muscles of mastication, there is atrophy of a greater degree than results from disuse alone. The same applies to the affected muscles in infantile paralysis. Atrophic tissues are much reduced in healing power and in resistance to bacterial infection. The latter not infrequently occurs in the processes of orthodontia, so that pressure must be temporarily relieved. Simple atrophy can be fully overcome with a return of the tissues to normal if the underlying cause be

removed. Secondary degenerations soon supervene upon atrophy under most conditions.

Cloudy Swelling.—**Causes of Cloudy Swelling.**—Cloudy swelling, also known as albuminous, parenchymatous or granular degeneration, is as the name indicates, a swelling of cells with a clouding of their boundaries and finer structure by albuminous granules (Fig. 22). The granules are soluble in acetic acid or alkali but not in ether and the fat solvents. As complex proteins their chemical nature is not exactly known and probably varies greatly under different conditions. Changes, structurally those of cloudy swelling occur within physiological variations. For example a glandular cell, over-

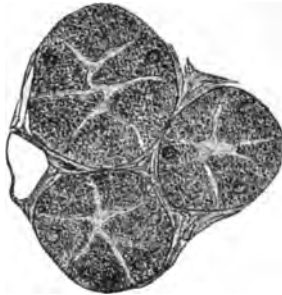


FIG. 22.—Cloudy swelling of cells of convoluted tubules of kidney. $\times 400$. (Ribbert.)

loaded with nutritional substances presents the picture of cloudy swelling, but chemically is probably different from that occurring in toxemia. Exhausted or starved cells show similar changes. The common cause of cloudy swelling is the poisoning of infections and inflammations. Exogenous poisons may cause the same changes, sometimes limited to certain tissues by selective action or at the organ of excretion such as the kidney.

Structural Changes.—In the gross the organ with cloudy swelling is slightly softer than normal in consistency and on cut surface is of a dull, lusterless gray color and more moist and opaque than normal. Microscopically in addition to granular clouding of the cytoplasm there are loss of the

limiting membrane of the nucleus, imperfect staining qualities of the chromatin and in the late stages vacuolation suggesting edema of the protoplasm. The glandular organs, especially the liver and kidney and the heart muscle, show this early degenerative change especially well. In the kidney it may cause albuminuria in a short febrile illness such as tonsillitis or abscess of the neck. This is not nephritis or Bright's disease. Recovery from cloudy swelling is complete if the cause is removed; if not it may pass on to fatty or other forms of degeneration.



FIG. 23.—Fatty degeneration of heart-muscle fibers, showing different grades of involvement of the individual fibers; fresh specimen. (Ribbert.)

DEGENERATION.

Fatty Degeneration and Infiltration.—Causes.—Fatty degeneration is the transformation of the protoplasm of the cell into fat. Fatty infiltration is the deposition of fat derived from the circulation in or between the cells (Fig. 23). A long controversy has been carried on as to which of these processes is the usual one. In many instances it is impossible to make any distinction. In general obesity, from simple overeating and lack of exercise, the excess of

fat in regions which normally have more or less fat may be regarded as fatty infiltration as also fat filling in spaces left in tissues undergoing atrophy. Fatty degeneration on the other hand is the result of poisoning much the same as cloudy swelling except that the process has gone further and is permanent. The metallic poisons, mercury, lead, arsenic and phosphorus and many other inorganic and organic poisons are powerful causes of this change. Chloroform anesthesia is sometimes followed by an acute and fatal fatty degeneration of the liver and other viscera. The most common cause of fatty change, however, is the toxemia of acute and chronic infections such as diphtheria, tuberculosis and chronic sepsis. Deficient oxidation is also a factor. Severe anemia is associated with fatty degeneration, but here toxic factors are usually present as well. Chronic alcoholism is a very potent cause. Finally metabolic disease such as diabetes may supply the necessary poisons.

Structural Changes.—In the gross, the fatty organ is enlarged unless an associated atrophy or fibrosis contracts it. It is also softer in consistency with rounded edges. The cut surface has a pale yellowish color and a greasy feel. Microscopically fine droplets appear in the cytoplasm of the cells. These may be identified by their solubility in ether and by their taking the fat stains—red with sudan III and black with osmic acid (Plate IV). Droplets may coalesce until the cell is nearly taken up by one large fat drop. The nucleus of the cell at first remains intact, later loses its chromatin and finally disappears. The cells thus destroyed are finally replaced by connective tissue. Fatty degeneration abounds in a great variety of combinations with other pathological processes, such as chronic passive congestion of the liver (nutmeg liver), atrophy, amyloid and other degenerations. It occurs especially in the liver in alcoholic cirrhosis, in the kidneys and other glandular organs and the heart muscle. Lipoid substances other than neutral fat such as oleates and cholesterin are found in these areas of fatty degeneration as shown by certain characteristics of refraction, so that the chemical process is probably a complex one.

PLATE IV

FIG. 1



Brown Atrophy.

Brown atrophy of heart, from section stained by hematoxylin, to show accumulation of reddish-brown pigment granules at either pole of the nuclei of the atrophic muscle fibres. (Adami and McCrea.)

FIG. 2



Fatty Degeneration.

Muscle fibres of heart from case of pernicious anemia, stained by Sudan III and hematoxylin to show fatty degeneration involving groups of muscle fibres. (Adami and McCrea.)

Amyloid Degeneration.—Cause and Chemical Nature of Amyloid.—Amyloid degeneration or infiltration, otherwise known as lardaceous or waxy degeneration may be defined as the deposition in and about bloodvessels and in interstitial tissues, of a glassy homogeneous glycoprotein substance giving characteristic microchemical reactions and most frequently resulting from chronic suppuration. The substance takes a mahogany brown color with iodine changing to violet or black with 10 per cent. sulphuric acid. This “starch-like” reaction was the origin of the term amyloid. The amyloid material, however, is a protein containing chondroitin sulphuric acid, which is related chemically to the chondrin of cartilage and tendon.

This may be carried in the circulation and diffused out through the vessel wall, where it combines with a local protein to form the amyloid substance. The latter is highly resistant to acids and is not digested by enzymes or decomposed by putrefactive processes. Etiologically it is associated with chronic suppuration and ulceration, especially in tuberculosis, syphilis, chronic osteomyelitis with bone sinuses, chronic sepsis and pyemia and intestinal ulcerations such as amebic dysentery. It may, however, occur in chronic intoxications without suppuration as in Bright’s disease. An excessive waste and discharge of leukocytes or other protein material is believed by some to be the indirect cause of amyloid disease.

Appearance and Distribution of Deposits.—In the gross, the organ with marked amyloid deposits is enlarged, has an increased specific gravity and is very firm and inelastic. The cut surface is glistening, waxy and translucent. The spleen shows amyloid particularly well. If the deposit is diffuse it resembles bacon and the term “bacon spleen” has been applied to it. If the deposit is focal, as it frequently is about the Malpighian bodies, the starch-like granules have given rise to the name “sago spleen.” Microscopically the amyloid substance is found just outside the endothelial lining of the capillaries and in the media of the larger vessels, also in the interstitial tissue around the vessels, so that the latter are

compressed. Connective tissue of the glands and of the intestinal mucosa and also muscle tissue are other localizations. Epithelium is not involved. Sections stained with methyl violet color the normal tissues blue and amyloid deposits light pink or red (Figs. 24 and 25).



FIG. 24.—Amyloid degeneration affecting the liver; slighter grade; the cells are still present with but moderate atrophy; the irregular deposit of amyloid around the capillaries is well marked. (After Ribbert.)

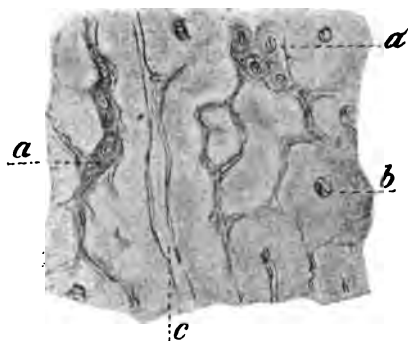


FIG. 25.—Amyloid degeneration of liver, advanced: *a*, atrophied liver cells; *b*, transverse section of a capillary surrounded by a broad ring of amyloid material; *c*, a capillary cut longitudinally. (Ribbert.)

Clinical Manifestations of Amyloid Disease.—Amyloidosis or extensive amyloid degeneration is really a disease in itself. In addition to the liver and spleen, which are practically always

involved in amyloid disease, the kidney, intestinal mucous membrane, adrenal glands, lymph glands and the larger blood-vessels show this change. It may also occur in localized form within infectious granulomata and malignant tumors especially in the region of the head and neck. It may be recognized clinically by the associated condition, mostly commonly chronic tuberculosis of lungs or bones, or syphilis and by the firm, enlarged and painless liver and spleen. When the kidney is involved the urine is increased in quantity, low in specific gravity and contains albumin and casts, the latter sometimes showing the amyloid reaction. High blood-pressure does not occur unless the ordinary form of Bright's disease is also present. Diarrhea is also a frequent accompaniment. The prognosis is bad because of the associated condition. The presence of the amyloid substance itself is relatively harmless and patients may live for years with extensive amyloidosis.

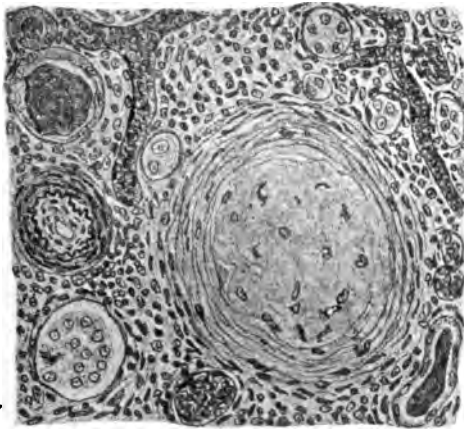


FIG. 26.—Hyaline degeneration of a glomerulus, from a kidney showing chronic interstitial nephritis. (Adami and Nichols.)

Hyaline Degeneration.—Causes.—Hyaline degeneration is the transformation of tissue into a clear, firm, structureless protein substance, which does not show any characteristic

reactions. It stains readily with acid aniline dyes and appears as a bright pink with eosin. The chemical character of hyaline substance is not known and is probably quite different in different locations. The staining qualities vary in the great variety of conditions under which this type of degeneration occurs. It is preëminently a change of the arterial wall and is very widespread in the vessels of glands and of the nervous system and in tumors. It occurs in the endocardium and in the heart valves and aorta and is closely related to the arteriosclerotic process of old age (Fig. 26). Muscle also shows hyaline degeneration, especially as a result of intoxications and septic processes. Other tissues may show it following cloudy swelling as a more advanced stage of toxic action.

Structural Changes.—Hyaline change is rarely massive enough to show any gross change other than that of increased fibrosis. Microscopically the pink areas are seen in the above locations as structureless, highly refractive masses, in which at most remnants of cell outlines and nuclei can be made out. The lumen of bloodvessels is narrowed or obliterated. This in certain tumors leads to impaired nutrition and changes in the cylinder of cells around the vessel, a formation which has been called *cyliindroma*. There will undoubtedly be a subdivision of hyaline degenerations with more exact knowledge of their chemical nature and origin.

Mucoid Degeneration.—**Chemical Nature and Appearance.**—Mucoid or myxomatous degeneration, strictly defined, is the transformation of cellular protoplasm into mucin, a glycoprotein with definite physical characteristics but of somewhat variable chemical composition. Chondroitin sulphuric acid has been found in it, so that it has some chemical similarity to amyloid substance. Mucin is insoluble in water but readily soluble in alkaline solutions. It is precipitated by acetic acid (the solvent of the granules in cloudy swelling) and by saturated solutions of salts. It has the capacity of absorbing considerable water but will not dialyze. The carbohydrate moiety of the glycoprotein reduces cupric sulphate in alkaline solution. Mucin is secreted normally from the glands of mucous membrane and from the salivary

and other glands. Pathologically it is most common in the connective tissues including cartilage and bone, but may occur in the epithelial cells of tumors and mucous membrane. It is widespread in the subcutaneous tissues in myxedema as described under thyroid disturbances. Polyps in the nose or its accessory sinuses show myxomatous degeneration. This may be regarded as a reversion of the connective tissue to the embryonic type as seen in Wharton's jelly of the umbilical cord. Mucin is deposited between the cells, which are compressed and assume spindle or star shapes with long anastomosing processes extending through the almost structureless matrix. Muroid tissue takes the basic aniline

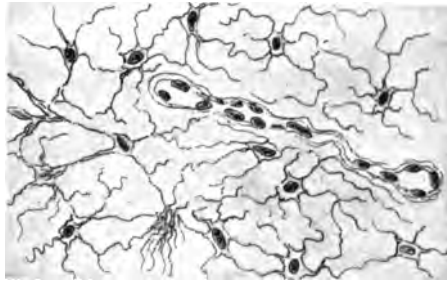


FIG. 27.—Section from typical portion of a mucoid polyp. (Collection of Royal Victoria Hospital.)

dyes such as methyl blue. There is only a very faint tint with eosin. Muroid tissue is of soft gelatinous consistency (Fig. 27). The mucin may be reabsorbed and myxomatous connective tissue may return to normal as in myxedema after treatment.

Colloid Degeneration.—**Ambiguity of Term.**—Colloid degeneration is a very inaccurately used term. It is applied to the colloid secretion contained in the acini of the thyroid gland and also to a modified mucin or pseudomucin occurring in tumors arising from mucous membrane such as cancer of the stomach (colloid cancer) and cysts of the lips. Thyroid colloid is a nucleoproteid and contains iodine. The latter secretion though similar in physical characteristics is a

pseudomucin. The name colloid is used when the appearance is that of the colloid of the thyroid. It is apparently due in some cases to compression of mucoid substance as indicated by compression rings in the mass within the acinus. The pituitary shows colloid substance in its thyroid-like structure. Colloid stains well with eosin, but not quite so strongly as the tissues in hyaline degeneration (Fig. 28).

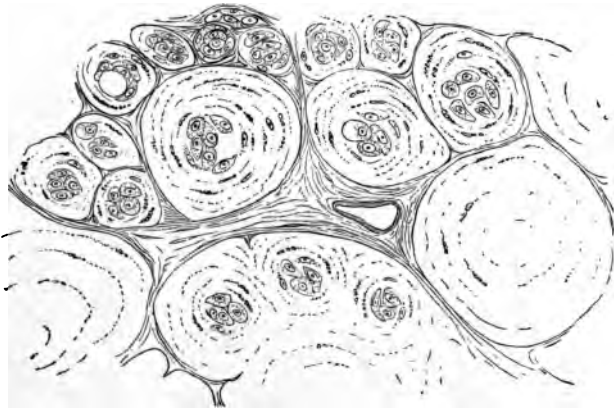


FIG. 28.—Colloid cancer, showing large alveoli with cell remains, within which is contained the gelatinous colloid material. $\times 300$. (Rhindfleisch.)

Allied Tissue Changes.—*Hydropic* or *Vacuolar* degeneration or serous infiltration implies an excess of fluid within the cells. It may be in the form of minute droplets, giving a granular appearance similar to cloudy swelling or it may be in large drops filling the whole cell and displacing the nucleus. (Fig. 29). It may occur as part of a diffuse edema or dropsy of the tissues as a result of various inflammations such as the vesicular skin diseases.

Glycogenic Infiltration refers to an unusual distribution or excessive deposit of the carbohydrate, glycogen which is normally present in the liver, muscles and most other tissues in smaller quantity. Normally it is stored carbohydrate food. It is found, however, in malignant tumors, in which physiological functions are lost. It occurs also in diabetes.

Microscopically it appears as clear colorless droplets within the cell. It stains brown with iodine, not changing to blue with sulphuric acid as the amyloid substance does.

Calcareous Infiltration or calcification is the abnormal deposition of calcium and magnesium salts in the tissues. It is a later stage of other degenerations, especially hyaline and fatty, in which the destroyed cells are replaced by calcareous salts. Like hyaline degeneration it is very frequent in the vascular system. The hyaline areas in the aorta

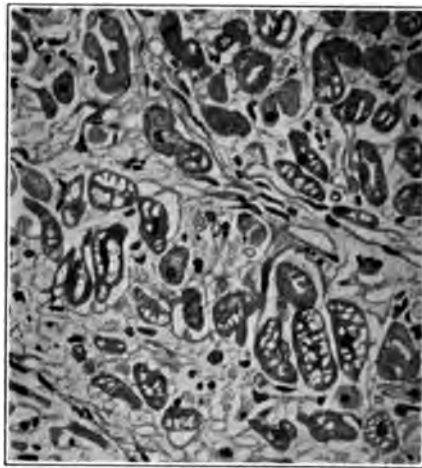


FIG. 29.—Hydropic degeneration of papillary muscles of heart which are cut transversely. The clear spaces indicate the vacuoles in the degenerated muscles. (Stewart.)

may become so calcified that the vessel is quite rigid. Sclerotic arteries may be calcified like pipe stems. In various inflammations such as tuberculosis, dead cells and scar tissue may be entirely replaced by calcareous deposits, which then really represent the last stage of the healing process. Within tumors also calcification frequently follows other degenerations. Microscopically the process begins in the form of fine granules in the intercellular substance. When they appear within the cell, it is usually dead or badly degenerated.

The granules stain a deep blue with hematoxylin. They later coalesce to form chalky deposits of considerable size. Sand tumors (psammoma) of calcareous material may occur in the central nervous system. Most extensive calcification is seen in extreme old age. Even the pulps of teeth may be calcified, filling the whole pulp cavity.

Ossification Contrasted to Calcification.—Ossification differs radically in that there is a formation of living bone tissue with the architecture of bone structure. It is brought about through the bone-forming cells or osteoblasts. Secondary bone, however, as well as secondary dentine is often very imperfect in its structure. There is sometimes a process of mixed calcification and ossification at the root of a tooth, so that it becomes quite ankylosed to the jaw. Extensive defects of the jaw may be filled in by secondary bone formation, especially if the periosteum is preserved.

Uratic Infiltration is simply the deposition of urates in the tissues mainly referring to the sodium biurate deposits of gout—the so-called tophi. The sodium biurate occurs as long slender needles microscopically.

Calculus Formation.—Calculi or concretions commonly called stones are formed by the deposition of salts of varying composition around a nucleus of foreign matter, including degenerated cells and bacteria. Calculi in the salivary ducts (sialolithiasis) are usually calcareous and may obstruct the duct or set up inflammation and infection. Gall-stones, kidney stones and calculi generally are formed similarly. Bacteria are frequently found in the center of stones. Oral sepsis may be the origin in some cases.

NECROSIS.

Definitions.—*Necrosis* is the death of tissue. *Caries* is a special form of necrosis. Death of individual cells is known as *necrobiosis*. Death of a part of the body including all the tissues is *gangrene*.

Causes.—Necrosis is the end-result of all the various degenerations, when the cause continues and the process progresses. The causes of necrosis therefore are the com-

bined causes of the degenerations. Any of the general extrinsic causes of disease, such as trauma, heat or cold if in sufficient degree may cause necrosis directly. In lesser degree preliminary degenerations occur. Depending on the particular conditions present, there may be several forms of necrosis.



FIG. 30.—Anemic infarct of cortex of kidney to show coagulation necrosis, with surrounding zone of congestion: *a*, artery. (Orth.)

Forms of Necrosis.—*Coagulation necrosis* is, as the name indicates, a death of tissue by coagulation. There is fibrin formation, as in blood coagulation and also other related proteid substances. The faint outlines of the cells without nuclei may be seen. The gross tissue is firm in consistency and pale and opaque. Coagulation necrosis may be produced directly by heat and is seen typically in infarcts, but

commonly is the result of bacterial poisoning. It is the earliest form of necrosis, in which there is the least structural disintegration of the dead cells (Figs. 30 and 31).

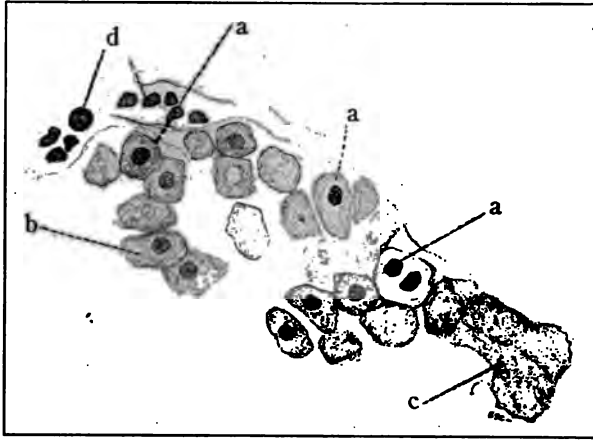


FIG. 31.—From a section of an adrenal gland, to show the gradations in cell damage leading to coagulation necrosis: *a*, adrenal cells still retaining nuclear stain; *b*, the same with fading of nuclear chromatin; *c*, completely necrosed cells seen as fused shadows; *d*, blood corpuscles. (Adami and McCrae.)

Caseation.—Subsequent changes lead to other forms of necrosis, such as *caseation* which is particularly characteristic of tuberculosis but occurs also in the gumma of syphilis and in tumors. Caseation refers simply to the cheese-like appearance of the necrotic tissue (Fig. 32). It has no constant chemical nature. Within the tubercle, coagulation necrosis occurs sooner or later from compression and the action of the toxins of the tubercle bacillus. In the center of this, caseation occurs as a more complete breaking down of the necrotic products. For example, a tuberculous lymph gland excised from the neck may show on section a pea-sized, soft, cheesy center surrounded by a firmer zone of coagulation necrosis.

Liquefaction necrosis or *colliquation* may follow other forms of necrosis such as coagulation or caseation. It is a solution

of dead matter by digestive ferments and in addition at times by bacterial action. Combined with caseation it forms a liquid cheesy material. All of the cell remnants may be destroyed so that clear liquid finally remains, which may be absorbed or become encapsulated or encysted as usually occurs in the brain. Caseous material when not liquified usually becomes calcified in the healed stage of the process.

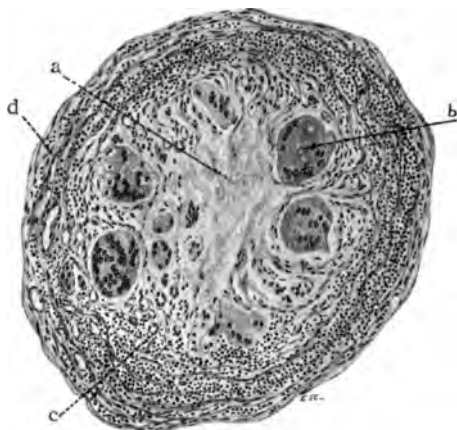


FIG. 32.—Tubercle from a case of tuberculosis, of medium severity, of the lung: *a*, central caseation; *b*, a giant cell; *c*, endothelial cells; *d*, connective-tissue zone infiltrated with lymphocytes. (Adami and McCrae.)

Fat necrosis arises independently of the other necroses by direct action of the pancreatic ferments on fatty tissue. The fat is split up by the steapsin into glycerin and free fatty acids. The latter is deposited in small white masses, usually not larger than a pea in the abdominal fat. It is associated with pancreatic disease, especially inflammation or obstruction of the ducts with escape of the pancreatic secretion. Gunshot wounds of the pancreas may be complicated by fat necrosis, which may extend beyond the abdominal cavity, by the diffusion of pancreatic secretion with the lymph. It is a very fatal complication. Microscopically, the crystals of fatty acid may be seen. Later they combine chemically

with lime and become encapsulated with a layer of fibrous tissue.

Focal necroses are multiple, minute areas of necrosis widely distributed in the body especially in the liver and kidney due to general infections and intoxications. The occasional cases of septicemia originating in abscessed teeth may show at autopsy numerous focal necroses. Microscopically they appear as small clusters of leukocytes and a few necrotic cells and bacteria. Actual suppuration occurs at times forming miliary abscesses. However, focal necroses are found in non-infectious toxemias. Capillary thrombosis may be the direct cause of the necrosis, together with the toxemia.

Gangrene.—Causes and Forms.—*Gangrene* is a rather general term for massive necrosis or death *en masse* of a part. A great variety of widely different causes may produce gangrene as stated under necrosis. Degenerations may precede actual gangrene or it may be primary especially when caused by virulent infections. There are two main forms—dry and moist.

Dry gangrene usually results from arterial obstruction as by embolism or thrombosis or advanced arteriosclerosis. If the process remains dry, the part becomes withered and very dark in color. This is called *mummification*. There is not much absorption from this form. A line of demarcation forms at the junction of the living and the dead tissues. The living tissues at the line are inflamed in response to an injury that is not severe enough to cause actual gangrene.

Moist gangrene is usually due to extensive venous occlusion with the edema that always follows. It may, however, result from many causes other than vascular lesions, especially severe infections. Infection may convert dry gangrene into moist gangrene and infection spreads rapidly. A foul slough or *sphacelus* is formed. This may be a diseased organ like the appendix or an extremity, usually the leg or it may occur in the center of a bone. A slough of dead bone as in the jaw from dental infection is called a sequestrum and the surrounding bone the involucrum.

Clinical Varieties.—There are many clinical varieties of gangrene of which the following examples may be mentioned:

1. *Senile Gangrene*—due to arteriosclerosis with increasing peripheral obstruction to blood flow and decreasing central pumping power of the heart. The circulation finally becomes inadequate to sustain the life of the tissues. It is of course apt to occur first in the most distant parts of the vascular system, namely in the feet. At first there are cramps. Then a purplish anesthetic spot appears. A vesicle forms over this region. The foot then darkens and the line of demarcation forms between the living and the dead tissues.

2. *Diabetic Gangrene* results from a nodular arteriosclerosis induced by diabetes and from the metabolic toxemia of the disease. Its onset is similar to that of senile gangrene.

3. *Inflammatory Gangrene* is directly due to the action of toxins, most commonly due to bacterial infection. The swelling and edema, always present in these severe inflammations, secondarily compress bloodvessels and conspire with the bacterial growth. This form may follow pneumonia. Gangrene of all of the superficial structures of the neck may result in severe infection such as Ludwig's angina.



FIG. 33.—Noma.

4. *Noma*.—A special form of gangrene is known as noma, which is a gangrenous stomatitis. It occurs most commonly in children with low general resistance following acute infectious diseases such as scarlet fever and measles. Extensive

foul sloughs form usually in the inner side of the cheek. Perforation and marked deformity result if the patient survives, which is exceptional. (Fig. 33).

5. *Emphysematous Gangrene* or gas gangrene is due to infection by gas-forming bacteria especially *Bacillus aërogenes capsulatus* and the bacillus of malignant edema. This occurs especially in war wounds, in which there has been soil contamination. The infection and gas are disseminated rapidly through the tissues and gangrene results from toxins and pressure. The emphysematous crackling may be felt on palpating the affected part.

6. *Carbolic Gangrene* is due to the direct toxic action of carbolic acid, which is a severe tissue poison. A dressing with 1 to 20 solution sometimes causes gangrene. Skin may slough and in the case of fingers, amputation may be necessary.

7. *Decubitus* or *Pressure Gangrene* may occur under too tightly applied splints or in the form of a bed-sore. The latter is usually seen in very sick or old people in whom the circulation is sluggish at best. Toxemia of disease may be an additional factor.

8. *Trophic Gangrene*.—The loss of trophic influence as in diseases of the brain and spinal cord or in broken back cases with paralysis also predisposes strongly to the so-called trophic gangrene. Some pressure is always present as well as circulatory disturbances. Mal perforans of locomotor ataxia is a trophic pressure ulcer occurring on the bottom of the foot or toe. Ulcer of the cornea readily occurs with the slightest trauma after extirpation of the Gasserian ganglion and loss of the trophic influence of the fifth nerve.

9. *Frost Bite* causes gangrene of toes, fingers or ears. The circulation is stopped by freezing.

10. *Raynaud's Disease* does the same by prolonged vaso-motor constriction.

11. *Thrombo-arteritis* of any kind has the same effect on the tissues involved. It may cause, as in leukemia at times, a localized gangrene of the tongue or lips, or in the larger vessels and associated with many diseases, gangrene of the intestine or an extremity. The numerous possibilities are seen without further examples.

CHAPTER XI.

INFLAMMATION.

Definition.—Inflammation is the succession of changes occurring in the defensive reaction of living tissues to injury. It is the most common of all pathological processes. In the evolution of the lower animals as well as of man, the tissues have acquired this mechanism to prevent extension of the injurious process such as bacterial invasion and to repair the damage done. The causes of inflammation are as numerous as the possible ways of injuring tissues. They are usually bacterial, traumatic or chemical. However, all of the primary extrinsic causes of disease considered under general etiology may lead to inflammation. Infectious inflammation may be steadily progressive because the causative agent is a living organism, which multiplies as the process advances. However, the essential features of all inflammation are the same. Infection may be and frequently is superimposed on traumatic and chemical inflammations because the damaged tissues have lowered resistance, and bacteria through the skin or mucous membranes, especially in the oral cavity, or through the blood stream, find favorable conditions for growth.

The Succession of Changes.—In following in detail the steps in the inflammatory process, it may be well to use the concrete example of a tooth with inflammation at the apex of its root, due to bacteria entering through a cavity, the pulp chamber and the root canal. The same changes may be directly observed by tying the toes of a live frog on the stage of a microscope and then injuring the web. Sudden injury causes a very transient vasoconstriction, which has no significance. The first step in the inflammatory reaction is vasodilatation primarily of the arteries, then of the capillaries

and veins (Fig. 27). This may be due to the vasodilator nerve fibers or to direct toxic action on the vessel wall. There is, in other words, an active hyperemia. After the first influx of blood there is a *slowing of the current*. The normal axial arrangement of the red cells within the vessels with a peripheral layer of plasma containing relatively more leukocytes is exaggerated. More leukocytes appear along the endothe-



FIG. 34.—Inflamed mesentery of frog: *a*, margination of leukocytes in the dilated capillaries; *b*, migration of leukocytes; *c*, escape of red corpuscles; *d*, accumulation of leukocytes outside the capillaries. (After Ribbert.)

lial wall. This is due to the chemical attraction or positive chemotaxis of the bacterial toxins in the case of the tooth infection. The endothelium becomes softened and the *leukocytes adhere* to it. The dilatation of the capillaries enlarge the intercellular spaces mechanically and the endothelial cells also show a vital activity in contraction and variation in shape, all of which increases the permeability of the endothelial wall. At the same time the ameboid move-

ments of the leukocytes under the influence of chemotaxis carry bud-like projections or pseudopodia through the intercellular spaces of the capillary wall. Soon leukocytes are seen in the tissue spaces outside the vessels. This is called *emigration*. The leukocytes in this active stage of inflammation are largely of the polymorphonuclear type. A few red cells, the number depending on the severity of the inflammation also find their way through the endothelial wall. This is *diapedesis*. At the same time plasma escapes and infiltrates the inflamed area. Fibrin ferment is liberated and strands of fibrin are formed so that a network completes the line of defense. While this defensive reaction on the part of the tissues is going on, bacteria, for example staphylococci in the tooth, are pouring down through the root canal and multiplying in the spaces about the apex.

The old analogy of an army of invasion, the staphylococci, meeting an army of defense, the leukocytes, applies very well. Casualties soon occur. Staphylococci are seen within the bodies of the leukocytes or phagocytes (eating cells) as they are now called. Other phagocytic cells, known as macrophages, large mononuclear cells probably originating from endothelial cells appear on the scene of battle. The staphylococci, the dead soldiers of the enemy are eaten by the phagocytes and soon digested by the intracellular ferments. However, the losses are not all one-sided. Many leukocytes succumb to the poisons of the enemy staphylococci either ingested or diffused in the serum all over the scene of conflict. The dead bodies of the leukocytes are sometimes carried off in the larger macrophages. The total wastage, dead bacteria, leukocytes and other cells and altered serum, is pus. Pus cells are the degenerated leukocytes. As the wastage accumulates in a central cavity, the contending forces are active at the sides and reserves are brought up in the rear. A dense massing of leukocytes organized in a network of fibrin forms a wall of defense, the abscess wall or pyogenic membrane. Ultimately either the army of defense or the army of invasion prevails. In the tooth almost invariably the defense prevails, especially when a dense abscess wall guards the apex of the root. However, the enemy is not

annihilated. Reinforcements are constantly coming down the root canal and a fighting infection may go on indefinitely until this communication to the outside world is removed, as by extraction. Sometimes the army of invasion succeeds either in the original attack or in subsequent attacks especially at times when the general resistance is low. Staphylococci then break through and meet the second line of defense in the lymph glands of the neck. Success here means an abscess of the neck. The fighting units on both sides have been increased enormously in number. The whole body responds from all parts and leukocytes increase to three or four times the normal number in the blood (leukocytosis). The poisons of the enemy are felt generally (fever and symptoms of toxemia). Free drainage and outlet of poisons at this point usually saves the defense. Occasionally and again usually when the general resistance is poor, the enemy staphylococci break through into the blood stream and are carried all over the body (septicemia) and the conquest is complete. The analogy is helpful in emphasizing the defensive nature of the inflammatory reaction.

Cell Types and Their Significance.—To return to the microscopic picture at the height of inflammation, there are dilated vessels and extravasated *polymorphonuclear leukocytes*, *red blood cells* and serum with strands of fibrin. The endothelial cells are swollen and take on phagocytic properties. In very acute inflammation, the pouring out of serum may amount to a marked inflammatory edema of the whole region. The tissue cells may show cloudy swelling or dropsical and fatty degeneration. The engorgement may be so intense that gross rupture of a small vessel causes hemorrhage by rhexis. All the colors of absorbing hemoglobin from yellow to black will then be seen in the later stages of the inflammation. *Lymphocytes* are relatively few at the beginning of acute inflammation but later as the polynuclears which survived the inflammation migrate through the lymphatic channels back into the circulation, lymphocytes take their place. They are derived partly by emigration from the bloodvessels but mainly from the regional lymphoid collections. They are only weakly phagocytic and have

practically no ameboid properties. In a low grade chronic inflammation lymphocytes predominate in the exudate from the start. As acute inflammation subsides, among the lymphocytes are seen many large mononuclear phagocytic cells, the above-mentioned *macrophages*, the origin of which is not very clear. They may be either altered lymphocytes or endothelial cells. They act as scavengers in carrying away pigments of all kinds, dead cells, blood pigment and other foreign material. Ferments derived from the leukocytes largely, are also instrumental at this stage in digesting the cellular débris. With this removal of the products of inflammation, the vasodilatation subsides or in other words resolution takes place.

Processes of Repair.—Defects in the tissues from the destruction of cells have yet to be removed. Connective tissue is always present. It is the least differentiated and the most actively reproductive of all tissues. New-formed connective-tissue cells appear as round or oval mononuclear cells which later become elongated to form fibroblasts and finally fibrous strands—the scar tissue resulting from inflammation. If there has been extensive destruction or an abscess cavity left after suppuration and discharge, an active proliferation of connective tissue and a low grade of inflammation go on until the loss is replaced. Lymphocytes abound in this stage and also at times plasma cells which are probably of lymphocytic origin although this is not settled. They are oval cells with an eccentric nucleus and a clear non-granular cytoplasm. In certain forms of chronic inflammation they are the predominant type of cell. In an abscess cavity, with the proliferation of connective tissue and endothelial cells, new-formed capillaries appear in great abundance. This is *granulation tissue* (Fig. 35). It bleeds on the slightest touch because there is only an endothelial layer of cells as the wall of the vessels. It is bright red in color and soon fills the abscess cavity, which also contracts with the subsidence of inflammatory swelling. Later by cicatricial contraction, the new-formed bloodvessels are gradually obliterated and the red scar changes to white. If for any reason complete healing cannot take place as occurs, when the

infection is not fully overcome, or when a foreign body is retained in the abscess cavity, there is an indefinite piling up

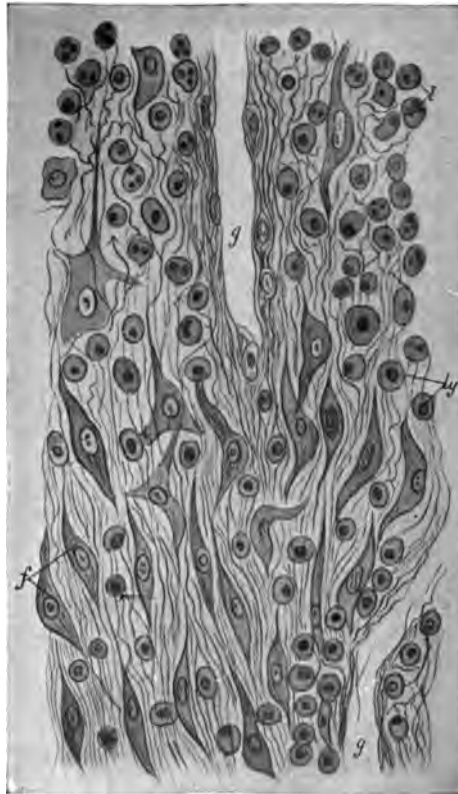


FIG. 35.—Granulation tissue seen from the deeper toward the upper surface: *f*, spindle cells (fibroblasts), most abundant in deeper portions, where they also are becoming shrunken; *ly*, lymphocytes; *g*, capillaries. (Ribbert.)

of an unhealthy granulation tissue or “proud flesh” with more or less purulent discharge. This occurs in the example of the abscessed tooth. The granulation tissue projects up

through the decayed tooth, which may become a mere shell containing the inflammatory tumor. If the alveolar abscess has discharged through the gum, granulation tissue appears at the fistulous opening and may remain there until the dead root is removed. Improved drainage through the root canal may enable the gum to heal, but after the infection is thoroughly entrenched in chronic form it is always uncertain whether it is obliterated without extraction or root amputation.

Symptoms of Inflammation.—The clinical manifestations of inflammation are best indicated by the ancient terms of Galen, *rubor, tumor, calor, dolor*, or redness, swelling, heat and pain. These are the cardinal symptoms, always present but sometimes much modified by the type and location of the inflammation. Another characteristic is usually added, namely *functio laesa* or altered function. Redness is due directly to the hyperemia. Swelling is also due to the excess of blood in the part, together with the extravasated serum and cells. The excess of liquid in the inflamed tissues served to dilute the toxins and facilitate cellular movements. Heat locally is due to the greater amount of blood and to increased chemical activity. Pain is produced by the action of toxins on nerve endings and, in parts that do not permit of much swelling, by mechanical pressure. For example, the tip of the nose and the concha of the ear are very painful when inflamed, even though they are fixed parts. The loose tissues of the eyelids permit of much more inflammatory swelling with less pain. Movable parts like the neck in turning the head or the tonsillar region in swallowing are painful when inflamed and at times the pain is referred through a nerve reflex to an uninfamed part. Pain from an infected third molar, or tonsillar abscess is often referred to the ear. The inflammation involving the nerve trunk frequently causes pain in the peripheral distribution of the nerve. For example involvement of the inferior dental nerve may cause pain in the chin or lower incisor teeth. It may also be referred in another branch of the nerve such as the auricular temporal and cause pain in the temple. Functional disturbances depend on the organ affected.

Glands may have diminished secretion with changed chemical composition. Mucous membranes have an increased and more viscid secretion. Muscle loses its contractibility to a large extent. Inflammation of the wall of the intestine in peritonitis causes paralysis of the muscle and a form of intestinal obstruction known as dynamic ileus. It is particularly the four cardinal symptoms of redness, local heat, swelling and pain that distinguish an inflammatory mass from other pathological processes. Certain types of inflammations especially the infectious granulomata produce localized swellings, which closely simulate true tumors. In the clinical differentiation it must be kept in mind too, that tumors and other pathological tissues may be secondarily inflamed.

Local Variations in the Inflammatory Process.—*Mucous membrane inflammations*, otherwise called catarrhal inflammations have certain special features. The first engorgement causes increased secretion of clear mucous (*mucous catarrh*). Soon there is some casting off of the surface epithelial cells (*desquamative catarrh*) causing turbidity of the mucus. Then the exudation of leukocytes into the secretion gives it the appearance in the gross and microscopically of pus (*purulent catarrh*). These stages occur regularly in the ordinary nose cold and in the simple inflammation of the oral mucous membrane. With more severe inflammation, there occur mucoid and fatty degenerations in the epithelial cells and some deposition of fibrin, in the meshes of which cells and debris are caught, forming a kind of membrane (*pseudomembranes, croupous or diphtheritic inflammation*) (Fig. 36). The term diphtheritic is used in a general sense, meaning membranous and not referring to the specific infection of diphtheria. Finally in the severest inflammation of mucous membrane as elsewhere there may be necrosis or sloughing (*necrotic or gangrenous inflammation*). The several terms represent different degrees rather than different kinds of inflammation. Other descriptive terms are used such as *hemorrhagic*, when there is considerable bleeding either by diapedesis or rhexis. In membranes, changed blood pigment may be quite black. *Productive inflammation* is characterized

by an overgrowth of connective tissue. This is usually a more chronic inflammation and in mucous membranes results in thickening and the formation of polyps. The popular term *catarrh* is no disease in itself. It is simply an inflamed mucous membrane, which may be due to many local or systemic causes such as an infection in the antrum or a chronic gastritis or pulmonary tuberculosis. Smoking is a common local cause of a low grade catarrh; chronic con-

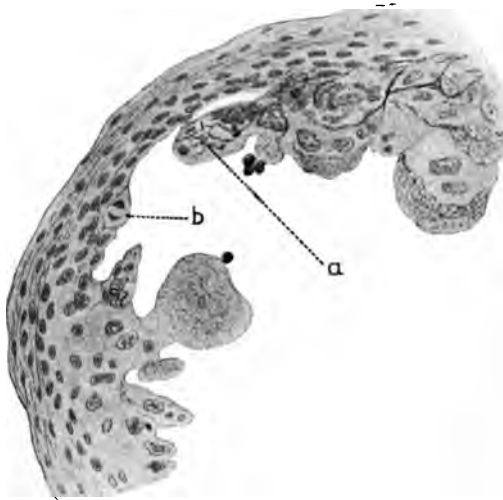


FIG. 36.—Wall of small artery with proliferating endothelium: *a*, phagocytic endothelial cells; *b*, attached endothelial cell undergoing mitosis. (Duval.)

stipation is a common systemic cause. An ulcer is due to necrotic inflammation of skin or mucous membrane. Its floor has the same construction as the wall of an abscess. Many descriptive terms are applied to ulcers, such as indolent, peptic (in the stomach), varicose and syphilitic. Mucous-lined surfaces do not adhere as long as the mucous membrane remains, even when actually inflamed. In such operations as closing a cleft palate, it is necessary to denude the edges

of mucous membrane so that healing may occur. It is part of the normal function of mucous membrane to maintain the patency of hollow organs.

Serous membrane inflammations also have certain special features, chief of which, in contrast to that of mucous membranes is the ready formation of adhesions. A fibrinous or plastic exudate is poured out on contiguous serous surfaces, such as the two layers of the pleura or two coils of intestine, and a firm union forms as the fibrin becomes organized to fibrous tissue. This is also a protective mechanism, since by it suppuration is limited instead of extending over a large surface such as the peritoneum. The latter is as large as the skin surface and when it is all acutely inflamed as in general peritonitis the patient is soon overwhelmed. If the infection originates in the appendix and is walled off by adhesions of the adjacent coils of intestine, the localized abscess thus formed may be safely drained. Pleurisy similarly causes adhesions between the two layers. With inflammation of serous membranes too, there is considerable pouring out of fluid exudate, always with an admixture of leukocytes, which distinguish it from a simple transudate. The character and number of cells in an aspirated fluid and its specific gravity have diagnostic value. An inflammatory process produces an exudate. Passive congestion due to heart failure causes a transudate with low specific gravity and relatively few cells. Serous membrane inflammations accordingly are described as fibrinous or plastic; serofibrinous, fibrinopurulent and purulent depending on the character of the exudate. Purulent exudate is pus. When confined in a cavity it is called empyema, whether serous or mucous membrane, for example pleural empyema or empyema of the antrum of Highmore or of the gall-bladder.

SUBACUTE AND CHRONIC INFLAMMATION.

Inflammation in other organs differs mainly in the disturbances of their special functions. It should be noted that the inflammatory process may be subacute or chronic from the outset, when the character of the exciting agent is not such

as to produce acute inflammation. Mild mechanical causes such as slight pressure or friction or the mere presence of a foreign body lead to chronic inflammation. At no time is there a marked exudation of polynuclear leukocytes. Lymphocytes predominate and fibroblastic proliferation starts at once. *Plasma cells* and not infrequently *eosinophilic leukocytes* are found. In the fibrous capsule formed around a foreign body such as a bullet, giant cells are sometimes produced. The infectious granulomata to be studied later are chronic inflammations from the outset. It is simply the nature of the specific bacterial toxin to affect the tissues in this way. It will be seen from the histology of the infectious granulomata, that they all have these essential features of chronic inflammation, although each disease has certain peculiarities of its own.

Summary of Sequelæ.—The sequelæ of inflammation are included in the following processes: (1) *Resolution*, (2) *suppuration*, (3) *ulceration*, (4) *fibrosis* and *scar formation*, (5) *necrosis*, (6) *gangrene*, (7) *cyst formation*, (8) *calcification* and (9) *regeneration* of parenchymatous cells.

REGENERATION OF THE VARIOUS KINDS OF TISSUE CELLS.

Regeneration after injury is somewhat stimulated by the injurious agent, so that an excess of new tissue is sometimes formed and subsequently absorbed. The regenerative power of different tissues varies widely from almost none in the highly differentiated cells, such as the ganglion cells in the brain, to a very free reproduction in the least differentiated which is connective tissue.

Surface epithelium regenerates readily since this is in the direction of its normal function. In an abraded area of skin or mucous membrane, epithelization proceeds from the periphery inward. The "taking" of skin grafts and their growth into new islands of epithelium on a raw granulating surface are evidence of the regenerative power of surface epithelial cells. This cell division may also be stimulated chemically as is seen practically under the application of

scarlet red. The bluish line at the edge of the epithelial growth advances more rapidly over the denuded surface than when unstimulated.

Glandular epithelium has distinctly less power of regeneration, but there is an attempt at cell division especially on the part of the duct epithelium. Typical acini are rarely reformed. Connective tissue fills in the defects.

Bone regeneration occurs as in the union of a fracture by first producing a marked overgrowth of connective tissue, the so-called soft callus, which surrounds the fragments. The more marked the displacement of the fragments, the larger the callus. Lines of ossification then form through the callus, which contracts and hardens. In malpositions of fragments, projecting edges are absorbed and permanent ossification is established in the line of stress upon the bone. There is no direct "knitting" or fusion of hard bone nor is there any need of great haste in setting a fracture because the connective-tissue callus is only slowly formed. If necessary a readjustment of fragments may be made after a few days without delaying healing. The least manipulation possible is of course always desirable.

Cartilage has comparatively little regenerative power. Most fractures through cartilage are replaced by fibrous tissue. Cartilage is also non-vascular and readily infected. Hence surgical wounds of election are made through bone in preference to cartilage.

Striated muscle has some power of regeneration, but it is not important in the healing of a cut or necrotic muscle. Union is mostly established by fibrous tissue. In this area, amitotic nuclear division may be seen and immature muscle cells without striation.

Smooth muscle often shows many mitotic figures after destruction of fibers, but here, too, a defect of any size is replaced mainly by connective tissue.

Blood and lymph cells are constantly regenerating. *Blood-vessels* are also readily new-formed as was seen in the organization of a thrombus or in granulation tissue.

Nerve cells do not regenerate; axis cylinders or nerve fibers may grow out after being divided. The distal segment

degenerates. The proximal segment connected with the nerve cell grows out if three necessary conditions are fulfilled: First, that the nerve cell itself is intact; second, that the path to the distal nerve segment is not lost by displacement or a scar tissue block; third, that the part supplied by the nerve has good nutrition and circulation. The operation of nerve suture is based upon this regenerative power of the cut axis cylinder. Accurate apposition of the cut ends enables the nerve connections to be reestablished. Different nerves may also be anastomosed, such as the proximal end of the spinal accessory into the distal end of the hypoglossal to overcome paralysis of the tongue. The results are, however, often disappointing.

CHAPTER XII.

SPECIAL INFECTIONS.

Individual Features of Special Infections.—There are a great many infectious diseases and the specific toxin of each one modifies the inflammatory process in a variety of ways.



FIG. 37.—Carbuncle.—Staphylococcus infection.

Under the heading of special infections, a few diseases may be considered to illustrate these modifications, the selective action of the different toxins and the resultant clinical features. The localized reaction to staphylococcus infection and the spreading character of streptococcus infection have

already been described and also the special streptococcus of erysipelas. Of other cocci, the gonococcus and meningococcus deserve special mention.

GONORRHEA.

Gonococcus infection is characterized by a severe and very persistent type of inflammation. The organism occurs intracellularly in diplococcus formation, two hemispherically shaped cocci facing each other. In culture there is only a scanty growth and that on special media. Infection is by

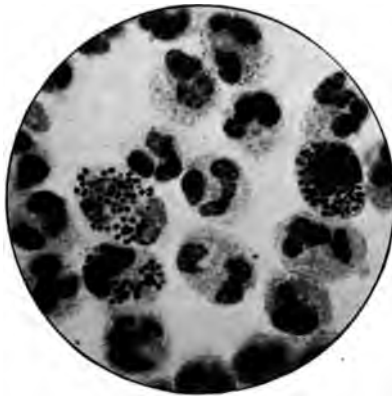


FIG. 38.—Gonococcus within pus cells, fuchsin stain. $\times 1000$ diameters.
(Fränkel and Pfeiffer.)

direct inoculation. The primary growth is practically always in the mucous secretions of the genito-urinary tract or in the conjunctiva. No other region seems to furnish favorable conditions for the primary growth of the gonococcus. It is almost unknown in the oral cavity although a few doubtful cases are reported. Other cocci may resemble the gonococcus morphologically very closely and may occur intracellularly quite like the gonococcus (Fig. 38). Without culture no definite statement can be made in doubtful cases. The conjunctiva of the eye, however, may readily be infected by contact with infected material or in newborn infants during

transit through the birth canal. This is ophthalmia neonatorum or gonorrheal conjunctivitis and ophthalmitis, which so frequently results in blindness. Gonococcus infection is ordinarily a purely local process but more frequently than in many other local infections, a few organisms are carried in the blood stream and set up secondary inflammations in other parts especially the joints. This is called gonorrheal *rheumatism*. It has a certain degree of predilection for the jaw-joint and may result in considerable ankylosis. The knee, ankle and articulations of the arm, however, are the ones usually involved. Occasionally the heart valves are attacked, causing an unusually severe form of *endocarditis*. Finally there may be a very fatal gonococcus septicemia. The secondary foci of infection are very obstinate. The joints not infrequently are swollen and inflamed for a year. The serious nature and unfortunate results of gonococcus infection, however, are in the great majority of cases due to the persistent local inflammation. The anatomy of the parts, the multiplicity of glands, from which drainage is difficult, favor the persistence of the infection for years. The structures most frequently harboring gonococci are the prostate and seminal vesicles in the male and the Fallopian tubes in the female. Sterility may result in either sex from purely mechanical causes—inflammatory and cicatricial occlusion in the epididymis or in the Fallopian tube.

Foci of Infection.—Chronic infection in these parts as elsewhere constitutes a focal infection and may cause a chronic deforming arthritis as well as abscessed teeth. The original infection may have occurred many years before and secondary infection by streptococci and other organisms may play a part in the late sequelæ. *Chronic gonococcus infection* may give rise to an acute infection as is seen only too often in newly married people. In women peritonitis may follow direct extension from the Fallopian tube. It may be fatal, but usually results in chronic tubal inflammation (salpingitis or "pus tubes") and general impairment of health. The dentist will rarely get a history of these conditions, but he should know that they are very frequent and not be too sure that in his patient with symptoms of focal infection, badly infected teeth are the whole cause.

CEREBROSPINAL MENINGITIS.

The *meningococcus* is morphologically indistinguishable from the gonococcus, but has a predilection for the nasopharynx and the meninges. It can be demonstrated by culture from the nose in cases of cerebrospinal meningitis and occasionally in those coming in contact with such patients. Many healthy carriers were thus found in military camps when the disease was prevalent. Crowding, fatigue and other conditions incident to camp life serve to lower resistance, and favor the outbreak of epidemic meningitis. The organism is believed to pass through the cribriform plate of the ethmoid to the meninges, but there is also often a blood infection to which the meningitis as well as arthritis and other complications may be secondary. There may be a nasopharyngitis as the initial infection and some of such cases do not develop meningitis, but serve as carriers to spread the infection. Accordingly the military dentist, especially in a camp where meningitis prevails, must consider the nasopharyngeal secretions of all patients as potentially infective. Although the specific antimeningococcus serum has reduced the mortality greatly, meningitis is still a very fatal disease. It sometimes occurs in the most extraordinary acute fulminating form, proving fatal within a day or two, but may also be very chronic, the meningococcus showing a persistence similar to that of the gonococcus. There is a suppurative inflammation of the meninges of the brain and cord, which obviously involves the cranial and spinal nerves. The resultant muscle contractures produce the characteristic symptoms of meningitis, namely, retraction of the head, flexion of the knees and later posterior bending of the spine (opisthotonos). This applies to any form of meningitis. The bacteriological differentiation must be made by examination of the spinal fluid obtained by lumbar puncture. Besides the meningococcus, the usual organisms causing meningitis are the pneumococcus, streptococcus, the tubercle bacillus and occasionally the influenza bacillus. All forms are more frequent in childhood.

TYPHOID FEVER AS A TYPE OF BACTEREMIC INFECTION.

Typhoid fever may be considered briefly as a type of a number of diseases, which are essentially generalized infections, although each may show certain features peculiar to the specific toxin at work. The bacillus typhosus is the specific and direct cause of typhoid fever. It may cause the disease in the most healthy individual but is frequently aided by predisposing causes such as fatigue, as in other infections. The portal of entry is the alimentary tract, the organism usually being carried in with water contaminated with sewage or with infected milk or food. The Peyer's Patch or lymph follicle of the intestine first shows the infection and reacts by marked inflammatory swelling (Fig. 39). The organisms readily find their way through the lymphatics into the blood stream causing a bacteremia, which is the essential pathology of typhoid fever. In about 75 per cent. of cases in the first week of the disease, the typhoid bacillus may be cultured from blood aspirated from a vein. In the majority of cases, some of the Peyer's patches go on to ulceration due to necrotic inflammation and vascular occlu-

LEGEND FOR FIG. 39.

FIG. 39.—Typhoid fever. Peyer's patches and solitary follicles from a youth, aged twenty years, to show the successive stages. (P. M. 31-08 Royal Victoria Hospital.) 1, Abnormally long Peyer's patch (16 cm.) showing congestion and slight swelling, in commencement of ileum, 250 cm. from valve. 2, Patch of normal size, situated a little lower down, 225 cm. from ileocecal valve, showing *état criblée*, and at a small area of hemorrhage; at b, another hemorrhagic area, with central pale-staining area of necrosis. 3, Patch, 210 cm. from valve. Here the solitary follicles also show swelling; at c, hemorrhagic areas with necrotic centers; at d, a loosened slough or necrotic area, bile stained. 4, Peyer's patch, some 50 cm. lower down with two sloughing areas, that at e, loose and almost detached; at f, solitary follicles, with necrotic centers. 5, A patch midway between the last and the ileocecal valve; g, hemorrhagic area; h, slough becoming loosened; i, ulcerated areas, from which the sloughs have escaped. 6, Large Peyer's patch, a few cm. above the valve, showing the completed ulcer. The whole patch has sloughed away, exposing the circular muscular coat of the bowel; m, solitary follicle that has ulcerated. There were ulcers also in the appendix, cecum and ascending colon.

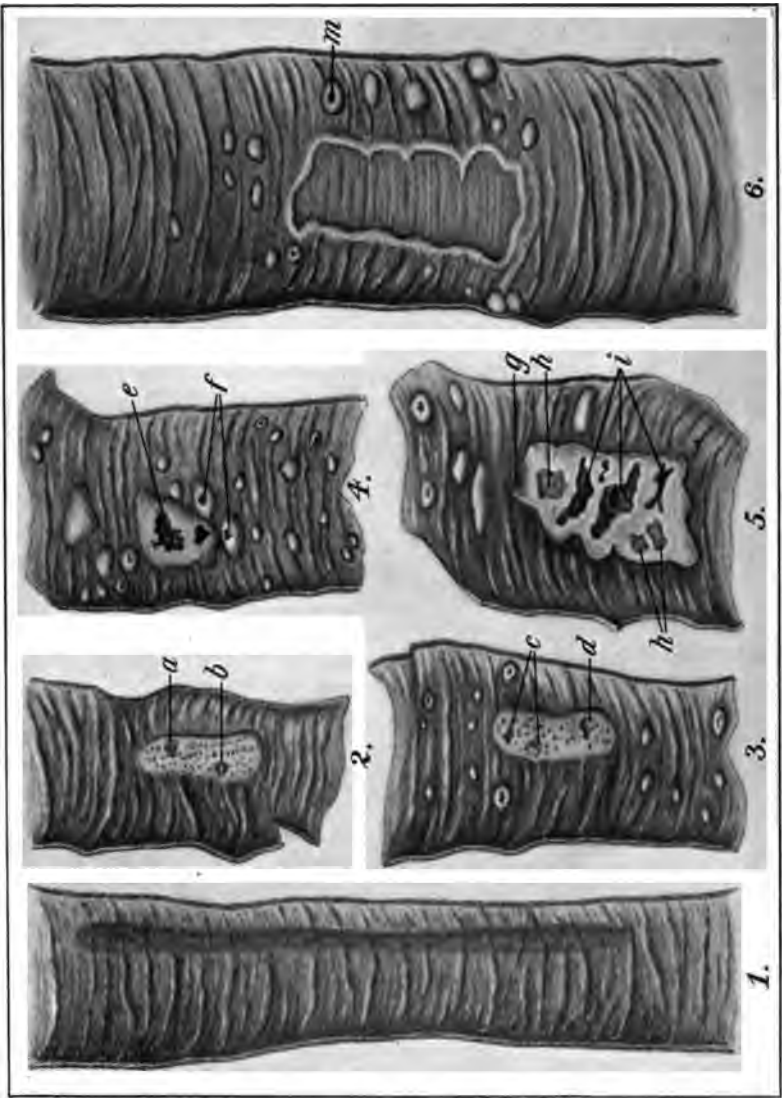


FIG. 39

sion from swelling of endothelial cells. This ulceration may open larger bloodvessels causing the intestinal hemorrhage of typhoid fever or may perforate the entire thickness of the intestinal wall and cause a fatal peritonitis if not promptly relieved by operation. However, the constant features of typhoid fever are due to the general infection and toxemia. This causes the fever, the coated tongue, the intense headache and muscular pains. The rose spots on the skin are localized hyperemias from which, by puncture, the typhoid bacillus can be cultured. At this time also, all the secretions and excretions may contain the organism, even the saliva. An initial bronchitis is frequent, with cough and slight expectoration. Some cases are ambulatory until the disease is well advanced. At times also the period of invasion may be drawn out over several weeks during which time, typhoid cases may come into the hands of the dentist. At the height of the disease the toxemia is frequently so profound as to cause a continuous fever of 104° or 105° and delirium or coma. The toxemia is the commonest cause of death.

Foci of Infection.—The bacilli carried all over the body in the blood stream may lodge almost anywhere and cause metastatic infection with or without suppuration. This is frequent in the gall-bladder, in the parotid gland, in the veins (phlebitis) or in bone. As the disease progresses, the natural defenses of the body assert themselves in the form of antibodies in the blood. These substances first inhibit the motility of the bacilli and then agglutinate them in clumps. This effect is seen by bringing the diluted blood serum of the patient in contact with a culture of typhoid bacilli in a hanging drop preparation under the microscope—the Widal reaction. The typhoid bacilli in this way are destroyed and the patient slowly eliminates the toxins and recovers. Most of the glandular organs pass through a prolonged cloudy swelling with focal areas passing on to more severe degenerations such as fatty and hyaline which are later replaced by connective tissue. Such damage is permanent and complete convalescence is very much prolonged.

Typhoid Carriers and Prophylaxis.—Moreover, certain resistant foci of typhoid bacillus infection remain indefinitely,

especially in the gall-bladder and intestinal tract and kidney. These cases are the typhoid carriers, which serve to perpetuate the disease. One attack usually confers a life immunity. The prophylactic inoculation with typhoid vaccine has been proved by army tests also to give a considerable degree of immunity. It consists in the hypodermic infection of 500 million dead typhoid bacilli followed at ten-day intervals by two more injections each of 1000 million bacilli. There is also a mixed vaccine containing the paratyphoid bacillus, a closely related organism, which produces the so-called paratyphoid fever, quite like true typhoid but in general running a milder course. Any one about to travel under conditions where he will be compelled to use drinking water and food of uncertain cleanliness would do well to take the prophylactic inoculation against typhoid fever.

TETANUS AS A TYPE OF ANAEROBIC INFECTION.

Tetanus or lockjaw is an important disease which may be considered as a type of the pathogenic anaerobic infections. It is a local infection with the *Bacillus tetani*, characterized by the production of one of the most powerful bacterial toxins known—so-called tetanospasmin which has a special predilection for nervous tissues. There is also a less important hemolytic toxin known as tetanolysin. The bacillus of tetanus abounds in cultivated soil and especially about horse stables. It is strictly anaerobic and bears spores which are resistant to a temperature that destroys other organisms and the tetanus bacilli themselves (Fig. 40). Growth is favored by the association of other organisms such as the pyogenic cocci which probably consume oxygen that otherwise would inhibit the anaerobic growth. In this way infected cuts of the scalp or hands may harbor a tetanus infection in the deeper tissues. Suturing such wounds favors the development of tetanus. *Puncture wounds* by soil, contaminated pointed objects, such as the proverbial rusty nail, present favorable conditions for the growth of anaerobic organisms. Puncture wounds through the mucous membranes, as in the mouth, may be infected as well as skin wounds. The incuba-

tion period varies widely, from one or two days to several weeks, and the infection may be stirred up much later by an operation in an old infected field. A short incubation means a virulent and fatal form of tetanus. The longer the symptoms are delayed the milder they are. The latter so-called chronic tetanus cases at times run a favorable course even without treatment. The tetanus toxin passes up the axis cylinders of motor nerves to the spinal cord. Muscle spasm may appear first in the vicinity of the wound but characteristically causes stiff neck and trismus. In acute cases generalized muscle spasm, convulsions and death rapidly follow. The therapeutic opportunity is in prophylaxis.



FIG. 40.—Tetanus bacilli with spores distending ends. $\times 1100$ diameters.
(Park and Williams.)

The affinity of the toxins for nerve tissue is so great that serum is of little avail after the onset of symptoms. It should be used at once after wounds such as broken jaw or war wounds of the mouth and especially puncture wounds and lacerations contaminated with soil. Local drainage and infiltration with peroxide of hydrogen may also be carried out. It is obvious that all materials injected hypodermically must be thoroughly sterilized, such as vaccines, gelatin solutions, paraffin in the correction of facial deformities and drug solutions. Tetanus is a local infection in contrast to the bacteremic diseases, of which typhoid fever was considered as a type. The general toxemia of tetanus is

mild even while the specific action of the tetanospasmin on the nervous system is overwhelming the patient.

Other pathogenic anaërobes are the gas bacillus (*bacillus aërogenes capsulatus*) and the bacillus of malignant edema found in gas gangrene wounds and the bacillus botulinus, the anaërobic organism mentioned under ptomain poisoning and "botulism." Vincent's angina is an anaërobic throat infection, which will be considered under the special pathology of the oral cavity.



FIG. 41.—One of the very characteristic forms of diphtheria bacilli from blood-serum cultures, showing clubbed ends and irregular stain. $\times 1100$ diameters. Stain, methylene blue. (Park and Williams.)

DIPHTHERIA AS A TYPE OF LOCAL INFECTION WITH SEVERE TOXEMIA.

Diphtheria is an aërobic local infection with a severe general toxemia as the main feature of the disease. It is practically always a throat or nose infection and its local manifestations will be described also in the special pathology of the oral cavity. The diphtheria or Klebs-Loeffler bacillus produces a soluble toxin, which is absorbed readily in the blood stream (Fig. 41). It produces early cloudy swelling of the glandular organs and especially of the heart muscle. These changes progress as the infection in the throat extends and the toxemia increases. Clinically the spleen enlarges, there is albumin in the urine and the heart sounds are weakened and irregular. Finally the heart muscle is paralyzed by the toxins of the diphtheria bacillus as the commonest

cause of death. In children asphyxia not infrequently results from mechanical obstruction to breathing in the larynx or trachea due to membrane and inflammatory exudate. This is relieved only by tracheotomy or intubation. Tracheotomy is the more generally applicable and usually the safer procedure in the various forms of laryngeal obstruction, especially in the presence of edema of the parts. The soluble diphtheria toxin stimulates the formation of antibody in the blood and the less virulent infections are overcome by the natural resistance of the body. The more virulent infections overwhelm the patient, before there is time for antitoxin formation in adequate quantity. Diphtheria is therefore a highly fatal disease when untreated by antitoxin. The latter is the serum of horses immunized by gradually increasing doses of diphtheria toxin. A broth culture from which the diphtheria bacilli have been filtered out contains the soluble toxin and on injection causes all the symptoms of the toxemia of diphtheria. By increasing doses at intervals a high degree of immunity can be induced in horses, so that many times the ordinarily fatal dose of toxin causes no symptoms. This process is called active immunization. When the antitoxic substances are simply transferred to a human patient by injecting the serum of an immunized animal it is passive immunization. Vaccine acts by active immunization depending on the patient's reactive power; serum acts by passive immunization. The latter in general is more suited to acute infections, the former to chronic infections.

Postdiphtheritic Paralysis.—Besides the ordinary toxin of diphtheria, which produces degenerative changes in the viscera, there is a special toxin with an affinity for the nervous system. It acts after the disease is overcome by causing paralysis usually in the palate, eye muscles or extremities—postdiphtheritic paralysis. It may occur in the milder cases of diphtheria. In fact it is sometimes the first suspicion of the true nature of a sore-throat which occurred several weeks before the onset of paralysis. Fortunately it usually clears up entirely. Certain individuals are normally immune to diphtheria. This may be elicited by the injection intradermally of diphtheria toxin (Schick test). If the patient

has immune bodies in his blood there is no reaction; if he is not immune a zone of hyperemia develops around the point of injection. Such individuals should have an immunizing dose of antitoxin when exposed to diphtheria.

Antitoxic Sera.—Special sera have been made for most of the infectious diseases, but only a few are satisfactory. Insoluble toxins or endotoxins held firmly in the body of the germ do not readily induce antitoxins that are useful in passive immunization. Some sera are bactericidal in their action. Serum and vaccine therapy will probably be much more highly developed in the future.

Other special infections may be studied in text-books of medicine. The above are sufficient to illustrate the pathological principles involved.

CHAPTER XIII.

INFECTIOUS GRANULOMATA

General Characteristics.—The infectious granulomata may be defined as infections characterized by a chronic inflammatory reaction and marked new tissue formation. As stated before they are only modifications of the inflammatory process due to the specific toxin of the causative organisms, which induces a slow proliferative reaction in the tissues. As might be expected this new tissue is largely connective tissue. This overgrowth is often in localized masses reaching considerable size, so that they have in the past been confused with true tumors. Now with the knowledge of their pathology and the discovery of the specific organism, such as the tubercle bacillus, they are recognized as being entirely distinct from true tumors or neoplasms. Clinically, however, at times, it is difficult to determine whether a given lump is a granuloma or a neoplasm until microscopic examination is made. The infectious granulomata then may logically be considered as intermediate between the simple inflammations and tumors. Tuberculosis, syphilis, actinomycosis, leprosy, glanders and rhinoscleroma are the classic granulomata. A closely related tissue change occurs in other chronic infections.

TUBERCULOSIS.

Etiology.—Tuberculosis in all its varied clinical forms and localizations is directly due to the lodging and growth of the tubercle bacillus in the tissues. The disease does not exist without this specific organism being present in every lesion. There are, of course, predisposing causes (as in all infections) which favor the growth of the tubercle bacillus by impairing the natural immunity of the body, but no hereditary predisposition nor any debilitating conditions or diseases can

PLATE V



Tubercle bacilli in red. Streptobacilli in blue.

X 1000 diameters.

cause tuberculosis in the absence of the tubercle bacillus. Before the discovery of the tubercle bacillus by Robert Koch, in 1882, tuberculosis of bones and joints, such as the familiar hip and spine disease, was often called traumatic inflammation and assumed to be due to injury. The history of injury, such as a fall in a child is always to be obtained at some time in the past—in fact is usually volunteered by the mother, and in the absence of a better explanation of the insidious disease the traumatic etiology was accepted. As a matter of fact the tubercle bacillus found its way from inhaled dust or milk or butter from tuberculous cows to the bony structures involved in the inflammatory process.

Bacteriology.—The tubercle bacillus is a long, narrow beaded organism, occasionally showing branched forms and frequently a parallel arrangement. It is acid fast when stained with carbolfuchsin, even prolonged action of acid (25 per cent. sulphuric) failing to break up the firm chemical union between the fatty substance in the tubercle bacillus and the dye (Plate V). Cultures on blood serum or glycerinated media, such as agar, potato or bouillon show a dry, wrinkled pigmented growth after ten to fourteen days. Tuberculosis occurs in many of the lower animals. The organisms adapt themselves to the conditions of growth in the different species. The optimum temperature for growth is the body temperature of the animal. Three distinct types are recognized (Fig. 42). The human, as above described, growing best at a temperature of 37°, the bovine growing best at 41° but more slowly than the human form and without the wrinkled pigmented growth characteristic of it, also showing a shorter, thicker organism with less heading—the avian growing best at 43° and in the form of moist, flat, luxuriant colonies. There is also a fish tuberculosis, the organisms growing best at only 24° and then much more rapidly than in the other forms. Only the bovine type is closely related to the human type. It has been established, contrary to Koch's original belief, that many of the infections in man are due to the bovine bacillus, especially in the bone and mesenteric gland tuberculosis of childhood. Obviously, milk for babies should come from tuberculin-tested cattle to be boiled

or dependably pasteurized before use. The tubercle bacillus is destroyed in moist heat at 60° C. for thirty minutes or 70° C. for ten minutes. The bovine bacillus is more virulent



FIG. 42.—Left lung, superior lobe, and upper part of lower lobe, the former containing a number of communicating caverns, brought about by tuberculous infiltration, caseation and evacuation of the contents through the bronchi. A, aneurysmal dilatation of an artery spanning one margin of a large cavity; B, communication with another cavity; C, C, thickened and adherent pleura between the two involved lobes. The pleura over both lobes is thickened, and at the autopsy the cavity had been obliterated by universal adhesion; D, a small group of tubercles in which caseation is just beginning; E, a fused group of tubercles, farther advanced than at D. (Hare.)

for certain animals such as rabbits and guinea-pigs than the human bacillus. In fact the latter injected subcutaneously is not pathogenic for cats.

Modes of Infection.—The portal of entry or atrium of infection in this great white plague in man is, of course, of great practical importance. In general it is the alimentary tract in children and the respiratory tract in adults. There is much evidence to indicate that the infection is usually acquired in childhood, even when the disease manifests itself for the first time in early adult life. The path from the intestinal tract to the thoracic duct and lungs is direct, so that bronchial gland and lung infection may result by way of the intestine as well as by inhalation of dust containing tubercle bacilli. With bovine infections the portal of entry is almost exclusively from infected milk. The human type of infection is similarly acquired by children living in infected houses. Infants living in the same rooms with tuberculous parents acquire the infection almost regularly. Contaminated hands and food carry in the organisms, which after passing through the intestinal wall may lodge and grow in the mesenteric glands—spread through lymphatic channels or be carried in the circulation to any part of the body. Conditions in the center of cancellous bone are favorable for the lodging and growth of tubercle bacilli, especially in the head of the femur and the bodies of the vertebræ, but also occasionally in the jaws and bones of the face. Infection may also occur directly from the mouth through defective teeth and especially through the tonsils to the cervical lymph glands.

The number of tubercle bacilli taken in as well as the resistance of the individual, determines whether tuberculosis becomes manifest at once, whether it is held in abeyance till a more favorable time, or whether it is blotted out entirely. Probably at least 50 per cent. of children under fourteen years (some European statistics show as high as 90 per cent. have harbored the tubercle bacillus at some time in their lives.

The organism is not transmitted from parent to child except in very rare instances of tuberculosis of the organs of

reproduction such as the placenta with which the fetal blood comes in close relation. The skin may be directly inoculated by the bite of a consumptive—by puncturing the skin with a pointed instrument as the finger of a dentist working in the mouth of a tuberculous patient. The postmortem wart or verruca is a tubercle on the hand acquired in autopsy work. Skin cuts by broken sputum glasses of consumptives have been infected. Skin inoculation in tuberculosis, however, is of little importance.

Immunity-Racial, Familial, Individual.—Immunity against such an omnipresent parasite as the tubercle bacillus is obviously of prime importance. Immunity or predisposition toward tuberculosis may be racial, familial or individual. Aboriginal races, such as the American Indian succumb rapidly to tuberculosis when the infection is introduced among them. Among civilized races, varying conditions of life, climate and many other factors in the development of the race have determined their particular degree of immunity to tuberculosis. No race is entirely immune. The disease abounds in North and South America, Europe and in the Orient. The various races represented in the immigrant population of the United States show their physical inheritance in this respect, in the percentage of tuberculosis among them. For example, the Irish in America have a very high morbidity and mortality from the disease. In contrast, the Russian Jews have a very low incidence of tuberculosis. The Latin races have considerable susceptibility; the Teutonic relatively less. The disease is very prevalent among the American negroes. Family predisposition is a much smaller factor than was formerly believed. A certain conformation of chest, the phthisical chest, a long flat chest with winged scapulæ has been regarded since the time of Hippocrates as predisposed to tuberculous infection. However, since most tuberculosis is acquired in childhood, much of this may be the result instead of the cause of the tuberculosis. Moreover, the most perfect type of chest may harbor the disease. Before the discovery of the tubercle bacillus, what little was known of the contagious nature of consumption was regarded as of secondary importance.

The great campaign of prophylaxis and education since then, although scarcely more than started has already yielded brilliant results. In other words, house infection before Koch's great discovery explained much of the family predisposition. Physicians frequently have occasion to see tuberculosis in a number of generations in the same family, such as a hunchback child of a tuberculous parent, an emaciated, consumptive grandparent with a history of a great-grandparent dying after years of chronic cough and hemorrhages. As stated, this is a matter of infection more than heredity.

Individual immunity is a considerable factor in the form of general bodily vigor and resistance to bacterial infection. Congenital disease of any kind, especially congenital syphilis, undermines the general resistance. Small children with bone tuberculosis in orthopedic hospitals show a rather surprising percentage of positive Wassermann reactions without clinical evidences of syphilis. If there is no actual infection transmitted at birth, however, Nature is very kind to the offspring. One frequently sees beautiful healthy babies from tuberculous mothers just as reclaimed infants of leprous parents may thrive normally in a sanitary environment. Disturbances of nutrition later in childhood, such as rickets, lower resistance to tuberculosis as well as to other infections. In adult life clinical manifestations of tuberculosis which are usually developments from the seed sown in childhood, frequently are determined by the degree of individual immunity. There is something in the physiology of early adult life and the period from eighteen to twenty-five years which permits of a higher incidence of pulmonary tuberculosis than at any other period in life even without other predisposing causes. During the prime of life tuberculosis rarely makes its first appearance. In old age the lowered general resistance again leads to an increase of the disease, in many cases, however, again a recrudescence of a process dating from youth. During adult life many factors reduce the individual immunity and act as predisposing causes of tuberculosis. Overwork, especially long hours of work, combined with poor food and dissipation and poor hygienic conditions

of living have always been considered large factors. Tuberculosis is preëminently a poor man's disease and its control is as much a sociological as a medical problem. Alcoholism has been a most potent factor, especially when combined with the above-mentioned conditions. Chronic diseases not infrequently end with a rather rapidly progressing tuberculosis. Bright's disease, diabetes and organic nervous diseases are examples.

Pathology of the Tubercle.—After noting the characteristics of the tubercle bacillus, the portals of entry into the body and the various body defenses against the infections, the lesion itself may now be considered. The tubercle bacillus, after having gained entrance into the tissues and lodged at a point favorable to its growth such as the center of a lymph gland, multiplies, produces bacterial toxins and excites a very characteristic type of cellular reaction in the adjacent tissue. These reacting cells around the organisms constitute the tubercle, which is the unit of the disease—identical in whatever organ or tissue of the body it may happen to be localized. The anatomy and physiology of the organ affected determine what the clinical disease will be—whether old-time consumption, or scrofula when involving lymph glands, or white swelling when affecting the joints or Addison's disease when the tubercles destroy the adrenal glands or tuberculous meningitis when the organism is carried to the central nervous system. The tubercle bacilli first of all set up a low-grade inflammatory reaction—a slight dilatation of the bloodvessels, a moderate exudation of serum and a slight exudation of leukocytes, mostly lymphocytes, but also a few polymorphonuclears. Most characteristic, however, is the proliferation of the connective tissue and endothelial cells of the tissue involved. These cells are called epithelioid cells because of their appearance. As tubercle bacilli die in the center of the tubercle and toxins are liberated there is a slow dry necrosis called caseation of the central mass. This is a structureless mass and acts as a foreign body in the tubercle. The irritation of this foreign substance as well as of the toxins liberated lead to the formation of giant cells—large multinuclear cells due either to the fusion

of a group of cells around a small mass of caseous material or of tubercle bacilli or due to nuclear division without cytoplasmic division. The nuclei of giant cells in tuberculosis are usually arranged peripherally. Although very frequent in tuberculosis, giant cells occur widely in the infectious granulomata, in true tumors and in the simple inflammatory reaction around foreign bodies. In the outer or older portions of the tubercle, the new-formed connective-tissue cells become elongated from fibroblasts to strands of

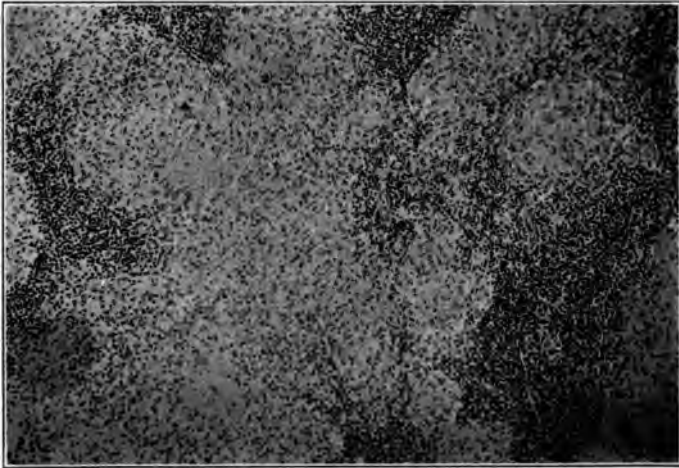


FIG. 43.—Tubercle formation.

fibrous tissue, forming a capsule for the tubercle. Diagrammatically, all these types of cells may be illustrated in a single figure (Fig. 32), although individual sections of tissue may show them quite incompletely.

Gross Results of Tubercle Formation.—Within the tubercle, the accumulation of tubercle bacilli and their toxins is determined by the resistance of the host. The cellular reaction may and often is quite adequate to destroy the colony of tubercle bacilli. The caseous material in the center is absorbed or infiltrated with lime salts, a form of healing

known as calcification. If the resistance of the host is not so good, tubercle bacilli migrate to contiguous tissues setting up daughter tubercles, which in numbers later fuse to form the so-called conglomerate tubercle. If tubercle bacilli are widely and rapidly disseminated in an area, there may be no discrete tubercles but a diffuse tuberculosis with a more or less uniform proliferation of the granulomatous tissue, the epithelioid cells being the characteristic feature. Organ-

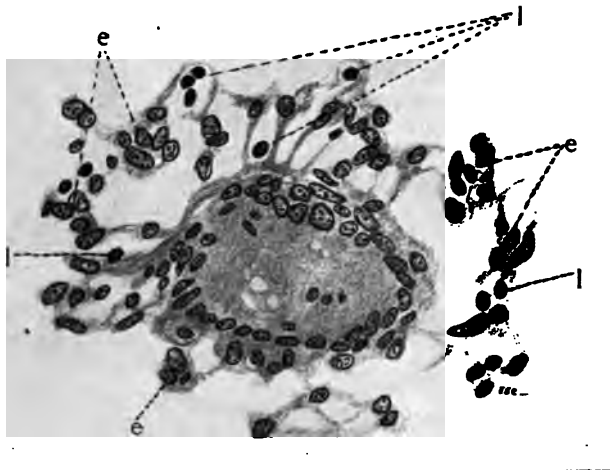


FIG. 44.—Giant cell from center of tubercle, showing processes and peripheral arrangement of nuclei, and surrounding endothelial cells (*e, e*) and occasional lymphocytes (*l, l*). (Adami and McCrae.)

isms may also colonize at a distance from their portal of entry by being transported in the lymph channels or blood stream. From the latter they may be filtered out in the kidney, where tuberculosis is practically always secondary to a focus elsewhere in the body. When there is rapid multiplication of tubercles, and extensive caseation as occurs in active pulmonary tuberculosis, cavities result from the destruction of tissue. When these communicate with bronchi there is profuse expectoration with tubercle bacilli in

the sputum. Erosion into bloodvessels leads to hemorrhage unless the vessels are thrombosed by the inflammatory reaction before their quite highly resistant muscular wall is destroyed. For the latter reason pulmonary hemorrhage from tuberculosis is not usually severe. Occasionally, an artery of considerable size traverses a cavity long after the destruction of the surrounding lung tissue. Aneurysmal dilatations may occur on such a vessel. It may finally rupture with profuse or fatal hemorrhage. Cavitation and hemorrhage may similarly occur in the kidney, liver and other organs.

Caseation—Tuberculous Abscesses.—Tuberculous caseation may lead to enormous quantities of this necrotic material, which is not pus strictly speaking, although having the gross appearance of greenish-yellow pus. It is sterile as far as pyogenic organisms are concerned and consists of the degenerated cells and tubercle bacilli. Only a comparatively few live tubercle bacilli are found. They remain in the more active areas in the walls of the cavity. This sterile caseous material accumulates and burrows along the channel of least resistance from its original source, such as a group of lymph glands in the neck or the body of a vertebra, and may travel a considerable distance along fascial planes, between muscles and under the skin. These accumulations are called *cold abscesses*, since there are no signs of acute inflammation as in ordinary abscesses. Acute inflammation may be superimposed on a cold abscess, which then quickly takes on the characteristics of an acute inflammation. This frequently occurs in tuberculosis of the lymph glands of the neck, the secondary infection gaining entrance from the mouth, most commonly through infected teeth or tonsils. A moderate enlargement of a lymph gland from tuberculosis may remain about the same size for many months and then when secondarily infected, suddenly produce a marked enlargement and an acute abscess. In this connection it may be pointed out that the reverse sequence of events may take place, especially in connection with infections in the mouth. The submaxillary lymph glands may be enlarged from simple chronic inflammation and as a point of localized

lowered resistance be secondarily infected with tubercle bacilli either from the mouth or from the blood stream.

Fistulae.—Tuberculous caseous material sooner or later finds an outlet. In the lung it discharges into a bronchus or bronchiole. From the spine it may travel down the psoas muscle within its sheath under Poupart's ligament and discharge through the skin in the thigh. In the neck it usually discharges directly through the overlying skin. Usually a fistulous opening remains. A persistent sinus leads up to a cavity in the center of a lymph gland. Secondary infection passes up directly from the skin. Tuberculous infection passes down the tract from the active process in the interior of the gland or wall of the abscess cavity. The sinus develops a thick fibrous wall and may persist in this form for months or years, discharging continuously or healing temporarily and breaking out again. The skin edge becomes undermined and several fistulous openings may form with an excess of scar tissue, giving the very characteristic appearance of the tuberculous sinus. This is the condition of the neck formerly known as scrofula.

Ulcers.—Tuberculous ulcers result from the lodging of tubercle bacilli on the surface of mucous membrane and occasionally the skin. Caseation and secondary infection lead promptly to sloughing of the surface layers of cells. The ulcers are pale pink, shallow and irregular in outline, slightly undermined at the edge and with a peculiar granular base. They occur in the mucous membrane of the intestine, kidney, bladder, bronchi, larynx, tongue, palate, and occasionally in the lips and cheek; the latter usually opposite a jagged tooth in a patient with tubercle bacilli in the sputum from pulmonary tuberculosis.

Acute Suppurative Tuberculosis.—Occasionally highly virulent tubercle bacilli set up a very acute suppurative process instead of the slower tubercle formation. True pus is formed, consisting of polymorphonuclear leukocytes and myriads of tubercle bacilli. A typical acute abscess results. This most commonly occurs in an individual of lowered resistance. After the acute abscess has drained out, the slower characteristic tubercle formation may go on in the old abscess wall.

Fibroid Tuberculosis—Lupus.—On the other hand, tubercle bacilli of low virulence, or in a host of high resistance may set up only a very slow overgrowth of fibrous tissue, which later contracts like all scar tissue and causes marked deformities and displacements in the affected parts. This is known as fibroid tuberculosis. In the lungs it causes the most extraordinary retraction and displacement of the heart, the trachea, the diaphragm and chest wall. Lupus or tuberculosis of the skin results also in marked fibrous overgrowth and contraction somewhat similar to that of a burn. It usually begins on the face, especially the cheek and nose and may extend to the mucous membrane of the mouth or nose. Occasionally it is primary in the mucous membranes and then most commonly in the nasal mucosa. Marked deformities and perforation of the septum may result.

Miliary Tuberculosis.—If tubercle bacilli are discharged into the blood stream from any focus, such as from a necrotic lymph gland eroding into a vein, there is, of course, a rapid dissemination of bacilli throughout the body. This causes the so-called miliary tuberculosis in which the organs are studded with innumerable small millet-seed-sized tubercles. Cut surfaces of the liver and spleen show them as fine white points. This overwhelming infection causes a high continuous fever not unlike that of typhoid fever and rapidly proves fatal. The rapidity of generalization of tuberculous infection, however, varies greatly. In the more chronic forms, there may be extensive involvement of bone, of the serous membranes and even multiple subcutaneous tubercles. Invasion of the meninges may be the closing scene. Tuberculous meningitis is uniformly fatal. This, like all forms of meningitis, is more frequent in childhood. Children living in poor hygienic conditions frequently fade away rapidly with acute generalized tuberculosis without a diagnosis. There may be no cough or suggestive symptom and the condition is frequently considered at first as a digestive disturbance.

Latent Tuberculosis.—Small foci of tuberculosis may heal and all the inflammatory products disappear, or be represented by a scar of fibrous tissue or, as mentioned above,

body. The resulting symptoms are loss of weight, disturbance of digestion, loss of appetite, anemia, weakness, rapid pulse, low blood-pressure and later fever and night-sweats. These symptoms may be present for a considerable period before localizing symptoms referable to any organ such as cough in lung tuberculosis, diarrhea in intestinal tuberculosis, pain in pleurisy, bloody urine in kidney tuberculosis, swelling in lymph adenitis in the neck or hoarseness in ulceration in the larynx. The latter symptoms illustrate the second group of *functional disturbances*. The third group are due to *mechanical factors*, such as pressure on the recurrent laryngeal branch of the vagus by a mass of tuberculous bronchial or deep cervical lymph glands producing vocal-cord paralysis. Pleurisy with a large serous effusion in the pleural cavity displaces the whole mediastinum, greatly compresses the lung and distorts the trachea and causes extreme cough and dyspnea.

Pulmonary Tuberculosis—Importance to Dentists.—The great majority of all cases of tuberculosis are of the only too familiar condition called consumption or phthisis, which is chronic ulcerative tuberculosis of the lungs. This has been a formidable scourge of humanity everywhere and yet is preventable by comparatively simple measures of prophylaxis. The only way to have these measures carried out, however, is by appreciation of the facts and intelligent coöperation on the part of the public at large. This means a great campaign of education, which is now well started. The modern dentist, with a knowledge of the general pathology of tuberculosis and its significance in public health, has a great opportunity for service by raising the standard of medical intelligence in his community. His close personal relation with people, often of the most teachable type in health matters, gives him a wide sphere of influence as the years go by. The early symptoms and modes of onset of tuberculosis should be kept in mind, since, as stated above, early diagnosis and treatment are second only to prevention. Any marked loss of weight should be a suggestion—the less reason there seems to be for such loss of weight, including the absence of all other symptoms, the more suspicious the case. There

may be headaches and neuralgic pains, and if the patient has just read of the relation of such pains to bad teeth he may go first to his dentist. Loss of weight is rarely absent when tuberculosis actively manifests itself for the first time. Later, weight may be regained and in chronic cases under favorable conditions patients may be quite well nourished. With the loss of weight there is more or less weakness, anemia and general subnormal health.

Modes of Onset.—There are a number of modes of onset with respect to the more specific symptoms. The most common mode of onset is with a *bronchitis*, which is especially suggestive in a young adult when it comes on insidiously without any acute head cold or grippe at the onset. It may, of course, be lighted up by such a cold and then continue indefinitely instead of running a self-limited course as a simple bronchitis would. Or there is a history of a tendency to “chest colds” on the slightest exposure. A *chronic pharyngeal catarrh* is often associated with this irritation lower down. Such conditions do not “run into” tuberculosis as is often popularly stated but are the result of a preëxisting tuberculosis. Obviously then, there is no nearly “going into consumption.” Either the infection is present or it is not present. Another frequent mode of onset is with *digestive disturbances*, loss of appetite, distress after eating and constipation. This is due to the toxemia of the disease. The stomach is the great mirror of the body; it responds to almost any toxemia or systemic disease. In these cases there may be no bronchitis, cough or any symptoms referable to the chest for long periods. If the patient recovers, there may never be any cough. Or the process may extend to a generalized miliary tuberculosis of the lungs as well as other organs and cause death without setting up bronchitis and cough. A third mode of onset is with *pleurisy*, which should always be regarded as tuberculous when it comes on unassociated with another disease, at least until another etiology is demonstrated. When pleurisy is secondary to another disease, such as pneumonia, influenza, inflammatory rheumatism, septicemia, or chest injury, the condition is apparent. Primary pleurisy is practically always tuber-

culous. Not every pain around the side of the chest is due to pleurisy, however. Lay people sometimes use the term as they use "rheumatism"—to mean any kind of a pain. Inter-costal neuralgia may simulate the pain of pleurisy quite closely. The latter, however, gives physical signs on examination. It may be dry with a fibrinous exudate on the pleural surfaces causing a wet leather creaking on breathing, or serous fluid may be poured out, producing the very characteristic pleurisy with effusion mentioned before. Pulmonary tuberculosis with predominantly pleural manifestations has always been regarded as having a somewhat more favorable prognosis than forms with bronchitis. There is no spreading of infection and the pleurisy frequently heals up permanently.

A fourth mode of onset is with *hemoptysis*, which may be the very first symptom. Hemorrhage is, however, more frequently associated with the late stages of the disease. In young adults, hemoptysis is rarely due to any other cause than tuberculosis. Occasionally a case of mitral stenosis causes hemoptysis because of the passive congestion in the lungs, but the heart lesion is apparent. Pneumonia, or a bullet wound of the lung, would be obvious. In older individuals a variety of conditions may lead to hemorrhage from the lungs, such as heart disease, aneurysm and tumors. Blood specks with mucous from the throat, of course, have no significance. A fifth mode of onset is with *laryngitis* and hoarseness. This also commonly comes in the latter states of the disease. Tuberculosis is rarely primary in the larynx, but not infrequently the laryngeal involvement produces the first definite symptoms, although there had been small foci in the lungs for a considerable period. Acute laryngitis clears up in a few days, or at most, a few weeks, so that when the hoarseness or aphonia lasts over four weeks it becomes very suggestive that it is more than a simple cold. It is usually one of three things, tuberculosis, syphilis, or in older individuals especially, a growth in the larynx. Tuberculosis of the larynx localizes first in the interarytenoid folds of mucous membrane where infectious material may lodge. Ulcers may then extend over the vocal cords up on

the epiglottis and to the pharynx. Dentists should know that in these cases of tuberculous laryngitis there are countless millions of tubercle bacilli in the sputum and that saliva is being constantly contaminated from the ulcers in the larynx by ciliary action as well as by cough and expectoration of purulent material. Finally, as a mode of onset, pulmonary tuberculosis may be preceded by involvement of lymph glands, especially of the neck. As mentioned before in connection with infection from the mouth, the lymph glands may be enlarged primarily from simple inflammation and as a "locus resistentiæ minoris" provide favorable soil for a stray tubercle bacillus or conversely tuberculous glands may be secondarily infected from the mouth with pyogenic organisms.

Methods of Diagnosis.—Tuberculin.—The diagnosis of pulmonary tuberculosis can usually be made by the time clinical symptoms appear and sometimes earlier by a careful physical examination of the chest. Inspection, palpation, percussion and auscultation furnish a multitude of physical signs to the trained observer. X-ray examination is of great help, but should always be correlated with the rest of the evidence in the case. When sputum is obtainable, the presence of tubercle bacilli is pathognomonic. In children especially, the tuberculin test is used. Tuberculin is a suspension of dead tubercle bacilli or an extract of their toxins. Several different preparations are used. When tuberculosis is present in the body, the tissues become sensitized to the toxin and react in the form of a local hyperemia when tuberculin is brought in contact with them. This may be done by applying a drop to an abrasion or puncture of the skin (von Pirquet test) or in the conjunctival sac (Calmette test) or by intradermal injection. Still more definite is the general reaction in the form of fever following in ten to twelve hours after a subcutaneous injection of tuberculin. One milligram is used in adults and if there is no reaction in a day or two, it may be increased to 2 or 3 mg. The tuberculin test is frequently positive in adults who are in good health with some old healed lesion, so that the test is of less value in adults than in children. Tubercu-

lin is also widely used to determine the presence of tuberculosis in cattle. Repeated injections in gradually increasing dosage build up an immunity, so that tuberculin is of some value in the treatment of tuberculosis, not as much as was originally thought, however. Then there are certain dangers in the use of tuberculin, since an overdose stirs up activity in the lesions of the disease.

Course and End-results of Pulmonary Tuberculosis.—The subsequent course of pulmonary tuberculosis may be rapid recovery or rapid extension and death or a chronic course of indefinite duration. Fibrosis, encapsulation and calcification occur in areas. Cavities may develop in other areas. If perforation of the pleura occurs at any point, air passes into the pleural cavity (pneumothorax) and the lung collapses. This is usually a serious complication, but at times it serves to control hemorrhage and profuse expectoration and absorption from a badly diseased lung, which is at the same time put at rest. In suitable cases pneumothorax is induced artificially by a needle through the chest, as a therapeutic measure. In chronic cases, amyloid and other degenerative changes develop in the organs. If the disease remains active, the patient gradually weakens and emaciates and sleeps away. Death is usually painless and consciousness may be retained until near the end. In some cases heart failure is the immediate cause of death, preceded by edema of the feet, dyspnea and all the signs of circulatory failure. Occasionally hemorrhage is fatal.

Distribution of Tuberculous Lesions in the Body.—Other localizations of tuberculosis in the body may be considered although pathologically the disease is identical wherever it occurs. In the *oral cavity* tuberculosis is surprisingly rare, and when it does occur is almost always a secondary process associated with pulmonary or laryngeal involvement. It occurs in the form of an ulcer on the *tongue, palate, lips or cheek* and usually at the site of a fissure or local injury, such as a bite. Tuberculous ulcer of the tongue occurs either on the dorsum or edge and has the characteristics of tuberculous ulcers elsewhere (Fig. 45). As in the larynx, it must be differentiated from syphilis and cancer. The

majority of cases will be seen in hopeless consumptives in the last months of their lives. The tonsils are not so often the site of actual lesions, but tubercle bacilli frequently lodge in the crypts and pass through to the submaxillary lymph glands. Below the mouth, the alimentary tract down to the small intestine is comparatively immune to tuberculosis. In the *lower ileum* particularly and the *colon* the characteristic ulcers again are often seen, extending



FIG. 45.—Tuberculosis of the mandible. (von Bergman.)

circularly around the bowel following the lymphatics. Occasionally they perforate causing acute peritonitis. They are also usually secondary to pulmonary tuberculosis in adults, but in children may be a primary infection. In the rectum these ulcers lead to secondary pyogenic infection and abscess in the *ischiorectal fossa*. As in tuberculous abscess in the neck, a persistent sinus results called fistula in ano. This may be due to simple infection, but about 25 per cent. of them are tuberculous. They are frequent in

chronic consumptives and may like the contracted scars in the neck serve as a suggestion that the patient has or has had tuberculosis. Tuberculous colitis may now be diagnosed by *x*-ray findings especially by hypermotility and filling defects.

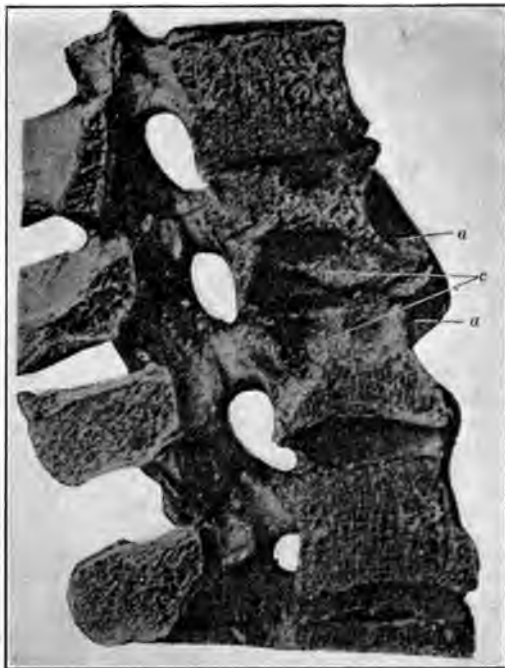


FIG. 46.—Tuberculous spondylitis (caries); *a*, osteogenesis and osteosclerosis; *c*, cavity formed by degeneration of tuberculous focus. (Kramer.)

In the *osseous system* there are also sites of predilection all more common in childhood. In the order of frequency the tubercle bacillus selects the hip, the spine, the knee, the ankle, the elbow, the sternoclavicular joint, the shoulder, the bones of the hand, of the face and occasionally of the jaws (Fig. 46). The malar bones and the superior maxillæ are more frequently involved than the mandible, and usually run a more

chronic course with discharging bone sinuses most of the time. In the mandible tuberculosis may be an extension from the disease in the mouth or tubercle bacilli may pass down through an abscessed tooth and result in a tuberculous osteomyelitis or it may occur as a metastatic infection from foci in the lungs or elsewhere. It is then usually part of a generalized infection with a very poor prognosis, so that radical local treatment is usually contra-indicated. Constitutional treatment leaving the mouth undisturbed so that the patient can take a full diet may be the wiser course for a period. When the general condition is satisfactory extensive removal of the tuberculous tissue down to normal bone is the necessary treatment. Sometimes the head of the mandible is necrosed in the temporomandibular joint by extension from a suppurative process in the middle ear, which occasionally becomes tuberculous in chronic consumptives.

The *genito-urinary* tract, as the channel of excretion of organisms, which have found their way from foci anywhere in the body, is frequently infected with tuberculosis—usually the kidney first. Secondary infection of the ureter, the trigone at the base of the bladder, the seminal vesicles and testicles is frequent. In the female, besides the urinary tract, the Fallopian tubes are often involved as part of a tuberculous peritonitis.

Relation of Tuberculosis to Dental Practice.—The dentist should know something of this great scourge, because it causes about 150,000 deaths annually in the United States alone, and because it will be present in some form in considerable numbers of patients that he works upon. It is one of the more frequent constitutional conditions that cause symptoms confusable with those of dental infection. Operative procedures quite proper in a normal individual may be quite unwarranted in the tuberculous patient. In a child, with tuberculous parentage and more or less delicate and anemic, it would be unwise to undertake a long-drawn-out and trying procedure in orthodontia. Even slight irritation in the mouth in such a case impairs the appetite, and thus lowers the general resistance.

SYPHILIS.

Etiology.—*Spirocheta Pallida*.—Syphilis is a specific generalized infection caused by the *Spirocheta pallida*, of slow evolution, and with four distinct stages. Although a chronic infectious granuloma-like tuberculosis, and in certain lesions resembling that disease very closely pathologically, syphilis differs fundamentally in that it is always a generalized infection. Wherever the spirochete is introduced into the tissues it steadily advances and in a few weeks is carried in the blood

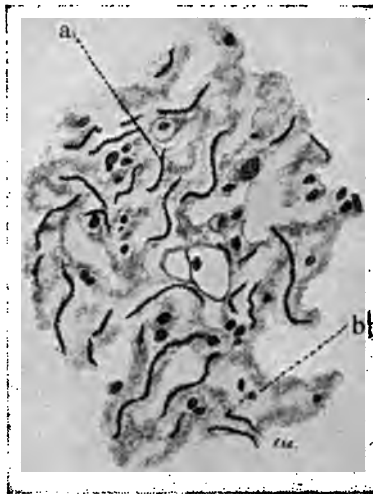


FIG. 47.—Spirochetes in liver of congenital syphilis (oil immersion): *a*, spirochete; *b*, nucleus of degenerated liver cells. (Adami and McCrae.)

to all parts of the body. The organism itself is a long thin spiral or corkscrew-shaped thread, very delicate, actively motile and non-refractile. It has from six to fourteen short regular turns—a feature which helps to differentiate it from other forms of spirochetæ. As its name indicates the *Spirocheta pallida* stains with great difficulty, except by special methods (Giemsa and Levaditi) (Fig. 47). In fresh material it may be seen best by the dark-field illumination. The organisms then stand out brightly against a dark background.

The *Spirocheta pallida* was discovered by Schaudinn in 1906. Only of late years has it been grown in artificial culture. Noguchi succeeded in finding a suitable culture medium containing tissue and diluted serum. The growth is slow like that of the tubercle bacillus, an average culture being obtained in ten to twelve days. The higher apes can be inoculated and Koch's postulates are fulfilled. Killed cultures of *Spirocheta pallida* have been used under the name of *luetin* by intradermal injection as a diagnostic test for syphilis comparable to tuberculin in tuberculosis, but so far it is not of much practical value.

Modes of Infection.—The atrium of infection in syphilis is through the skin or mucous membrane by direct inoculation with the spirochete usually in some slight fissure or abrasion or some break in continuity of the surface cells. Although usually acquired by sexual intercourse the disease can be acquired just as readily anywhere on the body surface if the infectious material comes in intimate contact. Accidental infections are only too common. Primary lesions occur on the lips from kissing, in the mouth, on the fingers, especially in doctors or dentists, on the nipples as of wet nurses on taking syphilitic infants and anywhere on the body of those living in conditions, where towels, dishes and clothing may be contaminated by people with open syphilitic lesions. The infection may gain entrance through the intact skin. Obviously, therefore, the disease cannot be considered a venereal disease, strictly speaking, but a general infection which is identical wherever the original portal of entry of the spirochete. In this respect it is like malaria, a blood infection, identical wherever the infected mosquito chooses to bite.

Congenital Syphilis.—Syphilis may also be hereditary or congenital. As a blood disease it is readily transmitted from mother to child. Syphilitic disease of the placenta leads to fetal death or premature birth, especially in the active stage of the disease (Fig. 48). Later the child may be born at full term but frequently dies early. However, the child may live and thrive normally or it may show signs of congenital syphilis at the time of the second dentition or in some other

PLATE VI

FIG. 1



Chancre of the Lip. (Brown)

FIG. 2



Mucous Patch. (Brown)

way. A history of a *succession of miscarriages* and stillbirths then is suggestive of syphilis, although it should be remembered that miscarriages alone may result from a variety of other causes. After a period of years, syphilitic parents, especially after proper treatment, may have normal children. Even without treatment, many children escape. Nature is kind to the offspring; not so kind to the syphilitic parent, who may go on to locomotor ataxia or some other later manifestation of his disease. Some of such children will have the disease in attenuated form, but in many it is impossible by any known means to find a taint. A mother without any clinical signs of syphilis bearing a syphilitic child cannot be infected by the child (Colles's law). An apparently normal child of an actively syphilitic mother cannot be



FIG. 48.—The teeth of hereditary syphilis at maturity.

infected by the mother (Profeta's law). The immunity in each case, however, is now regarded as being due to the presence of the disease in latent form since the blood test (Wassermann) is usually positive. These time-honored laws were based on clinical observation long before the discovery of the spirochete or of the relation of microorganisms in general to disease. Most infants with active congenital syphilis die early. Late congenital syphilis is relatively mild so that the practical importance of the disease is with the acquired form.

The Chancre.—The initial lesion of syphilis develops at the point of inoculation after a slow incubation of four to six weeks. It is called a hard chancre (Plate VI). Typically it begins as a small papule, sometimes as early as two

or three weeks after infection. This gradually enlarges and acquires a zone of induration around it of almost cartilaginous consistency. Hence, the term "hard chancre," which is used in contradistinction to soft chancre—a purely local disease with a short incubation period. Both infections may be present at once, however. The hard chancre usually ulcerates in the center and in the serum the *Spirocheta pallida* may be found in large numbers. There may be considerable edema around the initial lesion of syphilis. Small atypical chancres are not infrequent and are often entirely overlooked by the patient, but the systemic infection is the same. This has already taken place when the chancre has formed, as indicated by the indurated swelling and characteristic changes in the regional lymph glands. These so-called indolent buboes of syphilis rarely suppurate. The progress of the disease is slow. The chancre lasts about six weeks and leaves a persistent scar.

Pathology of Primary Lesion.—Pathologically, as the spirochetæ invade the tissues there results, as the most characteristic feature, a marked infiltration of small round cells. There is a low-grade inflammation. Epithelioid cells occur with proliferation of connective tissue. Giant cells may occur, but are not so constant as in the tubercle. Then there are changes in the small arteries and veins, mainly a thickening of the intima leading at times to an obliterating process in the vessel, and a denser infiltration of round cells around the vessels. Syphilis has a predilection for the vascular system generally and this perivascular infiltration of round cells is found in all stages of the disease.

Sometimes a chancre microscopically shows so dense a degree of round-cell infiltration as to be mistaken even by the experienced for a round-cell sarcoma. Staining the spirocheta, of course, identifies the process. This is the primary stage of syphilis and extends to the appearance of constitutional symptoms due to generalization of the infection—a period varying from six to twelve weeks after the appearance of the initial sore.

Secondary Syphilis.—The secondary stage is of the greatest importance to dentists because lesions in the mouth are

active and teeming with spirochetæ. The manifestations of secondary syphilis are as follows:

1. *Lesions of the Mucous Membrane.*—The throat reddens and becomes sore. So-called mucous patches appear in the pharynx on the tonsils, palate, cheek, tongue and lips—sometimes slight and limited to the pharynx—sometimes all over the mouth. They are flat, grayish, irregular patches of a semitranslucent appearance as if the mucous membrane had been lightly pencilled with silver nitrate. The tonsils are swollen and frequently show patches or small ulcers—sometimes white spots in the crypts like follicular tonsillitis but differing in the more chronic course. Acute tonsillitis subsides in three or four days. There is a diffuse catarrh of the oral mucous membrane, extending to the larynx causing hoarseness, and to the middle-ear causing deafness in greater or less degree. The cervical lymph glands are enlarged and tender and remain so for some weeks if untreated. Around the anus there are moist raised patches called condylomata. *Mucous patches* are highly infectious. Patients in this stage should be hospitalized for intensive treatment and the protection of others. Dental work during this stage can only be regarded as highly dangerous for the dentist. Pointed instruments and sharp edges of teeth make very efficient inoculators. If dental treatment is necessary, as for instance, to enable the patient to tolerate adequate mercurial treatment, rubber gloves should be used and care taken to avoid puncture through them.

2. *Lesions of the Skin.*—With the sore-throat appears also the characteristic rash on the trunk, back and arms, also on the face, especially along the hair-line of the forehead (*corona veneris*). It is in the form of reddish or copper-colored macules or blotches a quarter to a half inch in diameter. This eruption varies greatly in intensity. Sometimes it is so slight as to escape the notice of the patient, sometimes very marked and widespread over the body. There is no itching as a rule. The rash lasts two or three weeks if untreated and sometimes leaves areas of pigmentation, lasting for months. The rash may also recur. Falling out of the hair at this stage is frequent.

3. *The Lymph Glands* are enlarged to a moderate degree all over the body from hyperplasia due to the systemic infection. Those draining the throat may be as large as walnuts.

4. *Constitutional Symptoms*.—Fever, usually only one or two degrees, so that the patient is up and around although rather uncomfortable with headache, joint pains and general malaise. Occasionally the fever is high and the patient quite ill. Considerable anemia may develop as the secondary stage progresses. The joints are at times actually swollen as in mild rheumatism. Iritis is common. Redness of the eye, cloudy iris and distorted pupil serve as suggestions of syphilis but there are other causes of iritis, such as abscessed teeth and other focal infections. Lumbar puncture shows an increase in the number of cells in the cerebrospinal fluid in the majority of cases, so that there is an invasion of the nervous system early in the disease. Facial paralysis occurs occasionally. It is, however, more commonly not a syphilitic manifestation. During the secondary stage the spirochetæ are disseminated throughout the body as a true septicemia. Their virulence becomes attenuated and the secondary lesions disappear even without treatment, but the spirochetæ remain in foci almost anywhere but especially in the liver and other viscera, the aorta and the vascular system generally, the osseous and nervous systems, where later manifestations of the disease may occur.

Tertiary Syphilis.—The tertiary stage of syphilis is not sharply demarcated from the secondary. At any time after the height of the secondary symptoms and throughout the remaining years of life tertiary manifestations may occur. The characteristic lesion of this stage is the *gumma*. Pathologically it is quite similar to the tubercle. It shows round-cell infiltration, not infrequently giant cells and caseation at the center. Around the periphery there is marked fibroblastic proliferation forming a dense capsule for the gumma. The bloodvessels show the intimal thickening and perivascular infiltration of round cells, so characteristic of syphilitic lesions everywhere. The overgrowth of fibrous tissue and subsequent contraction are very marked in the

gumma, so that the caseous material is finally absorbed and nothing is left but a stellate scar. Multiple gummata in an organ are more apt to be in a similar stage of development than tubercles. The latter may be found in all stages mingled together. The spirochetæ are much less numerous in gummata than in the primary and secondary lesions, but do occur and inoculations of gummatous material



FIG. 49.—Syphilitic ulceration of soft palate. (Grayson.)

into apes have caused syphilis, so that the tertiary lesions must also be regarded as infectious. Gummata occur in the skin, in the throat, especially the tonsillar region, palate and tongue, and very frequently in the nasal septum leading to perforation; also in the periosteum of bones such as the shin, the sternum, the skull, especially the frontal bones, occasionally the jaws, finally in the muscles, notably the

sternocleidomastoid and in the internal organs. Gummata on the mucous membranes break down early and form ulcers with a characteristic "punched out" appearance—crater-like with perpendicular edges and relatively little inflammation around them (Fig. 49). In the soft palate they may cause a perforation, or on healing leave stellate scars, which



FIG. 50.—Gumma of shin.

are very characteristic of syphilis. If promptly treated they may heal with no scar. In the tongue chronic ulcers may form, which as stated before, resemble tuberculous ulcers, or in older people, cancerous ulcers. Gummatous lesions sometimes develop at the site of an operative procedure in the nose or mouth of untreated syphilitics, especially in operations on the nasal septum, which may slough out



FIG. 51.—The circinate squamous syphilide. (Jackson, courtesy of Dr. S. D. Hubbard.)



FIG. 52.—Bulging of the chest wall, with erosion of ribs, from aortic and innominate aneurysm. (Hare.)

entirely. Ulcers on the shins not due to varicose veins or to injury are usually syphilitic (Figs. 51 and 52).

Distribution of Late Syphilitic Lesions.—Tertiary manifestations of syphilis are varied and widespread. The *arterial system* is particularly vulnerable and from the disturbance of circulation any organ or structure in the body may be affected. The root of the *aorta* and the aortic valves are often the site of a syphilitic process causing one of the common forms of *heart disease*. The diseased walls of the aorta may yield to the intra-arterial blood-pressure causing dilatation of the aorta or aneurysm. Aneurysms reach enormous size at times, press on surrounding organs and may finally rupture. They may occur in the carotid arteries, producing an expansile pulsation in the neck. Aneurysm is almost always syphilitic. A few are due to trauma, such as a bullet wound injuring the wall of the artery. *Bone syphilis* is most commonly in the form of a periostitis, which shows in the x-ray as a diffuse thickening with a very characteristic wavy outline to the edge of the bone. Syphilis of the *central nervous system* or cerebrospinal syphilis is a most important condition and may produce almost any kind of symptom referable to the nervous system. It is frequently localized at the base of the brain and involves the *cranial nerves*, especially those of the *eye*, causing disturbances of vision, even blindness and strabismus or squint from paralysis of the extrinsic muscles of the eye. The facial nerve may also be involved, causing facial paralysis. An intense, persistent headache often occurs. Cases have occurred in which syphilitic headache was erroneously attributed to abscessed teeth resulting in misfortune to the patient. The untreated syphilis may eventuate in *paralysis* of one side of the body, loss of speech or epileptiform *convulsions* or almost any nervous accident. A so-called "stroke of apoplexy" in a person under thirty-five years of age, previously entirely well, is always strongly suggestive of syphilis. If the patient has had endocarditis he may have a cerebral embolism which would cause the same symptoms. Further detail would be out of place here for as the common saying has it "syphilis can do almost anything."

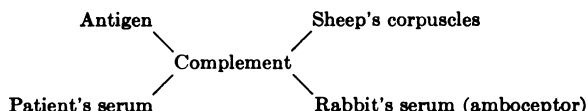
Quaternary Syphilis — Tabes and Paresis. — Quaternary stage is applied to the late degenerations in the nervous system as a result of the chronic infection and poisoning of syphilis. It is in two forms—locomotor ataxia or tabes dorsalis when involving the spinal cord, and paresis or dementia paralytica when involving the brain. The spirochete has often been found in these late lesions, which may come on from three to thirty years or more after the primary infection without any manifestations in the intervening years. Destruction of nerve cells is permanent, since they have no power of regeneration, so that these lesions once established are hopelessly incurable. The lesion of locomotor ataxia is an atrophy and sclerosis in the posterior root ganglia and the posterior (sensory) columns of the spinal cord. As might be expected from the physiology of these parts, the first symptoms are the so-called "lightning shooting or root pains" down the limbs and around the body from irritation in the posterior ganglion and root and mainly the sensory paralysis. Motor power is good, but the muscular sense of position and control over the limbs are lost. Skin sensation is impaired. Control of the sphincters of the bladder and rectum is gradually lost. The patient, however, may live for a number of years in this condition. Their resistance to simple infection is much reduced. Processes of repair are uncertain. Fractures sometimes occur with slight violence and often fail to unite. Operative work must be of the simplest character. Paresis supplies a certain percentage, approximately 10 per cent. of the inmates in insane asylums. It comes on with changes in personality, talkativeness, delusions of grandeur, the patient imagining himself wealthy or powerful. Later there are excesses of all kinds, tremors and ultimately complete dementia and paralysis. They rarely live longer than three years after the onset of symptoms. The higher centers of the brain show similar pathological processes to those in the cord—infiltration, atrophy and fibrosis.

Lesions of Congenital Syphilis.—Congenital syphilis, in the common form, manifests itself as a nasal catarrh about the fourth to the eighth week of life, causing the so-called

"snuffles." It frequently leads to necrosis of the nasal bones and a depression at the root of the nose—the *saddle nose* which is so characteristic of congenital syphilis. The catarrh may extend to the middle ear and cause deafness. At the second dentition the *Hutchinson teeth* are characteristic. The upper central incisors especially are peg-shaped, stunted in length and breadth and narrower at the cutting edge than at the root and with a single notch at the cutting edge. Here the dentin is sometimes exposed and the spirochete has been found in the tubules. Finally, the steamed or ground-glass cornea of *interstitial keratitis* may show up in the eye as a later evidence of congenital syphilis. This may develop about the age of puberty if not before. Late lesions may develop but are not frequent. In children the group of defects in nose, ears, teeth and eyes should be kept in mind. Open lesions may be highly infectious.

Wassermann Reaction—Complement-fixation.—The Wassermann test on the blood serum or other body fluid is an application of the complement-fixation reaction now quite widely used in laboratory diagnosis. It is simple in principle but quite delicate and difficult in technic. To understand it, it is necessary to understand the steps in the process of hemolysis. The blood serum of certain animal hemolyzes or lyses the red blood corpuscles of other animals, or may be made hemolytic for these foreign corpuscles by a series of injections of the corpuscles intraperitoneally into the animal. For this purpose sheep's red cells are injected into rabbits. The rabbit's serum will then hemolyze the sheep's red cells. In the process of hemolysis there always enters a substance called complement, which is normally present in serum and acts as a connecting link between the hemolytic serum (amboceptor) and the red cells. This complement is thermolabile, that is, it is destroyed by heating to 56° for a half hour. The heated or inactivated rabbit's serum then cannot hemolyze the sheep's red cells since complement is lacking. Upon the addition of complement from any normal serum hemolysis takes place. This is the so-called hemolytic system. The other system consists of antigen—an extract of syphilitic liver (cholesterin or extracts of normal

organs may be used), the syphilitic antibody in the patient's serum (inactivated) and a known complement contained in serum of a guinea-pig. These three, antigen, patient's serum and guinea-pig serum are incubated together at 37° for one hour when the complement is fixed and cannot combine with the hemolytic system of sheep's cells and rabbit's serum when incubated with them. The absence of hemolysis then means a positive Wassermann reaction. Presence of hemolysis means a negative Wassermann reaction, since there was no syphilitic antibody to fix the complement, which then was free to complete the hemolytic system of sheep's cells and rabbit's serum. It may be simplified as follows:



Complement combines to left in a positive test and to the right in a negative test. All these units must be carefully standardized, since the Wassermann is a quantitative test. Doubtful tests should always be repeated. A negative test does not always mean the absence of syphilis since many late cases will give a negative Wassermann. In active secondary syphilis it should be positive in nearly 100 per cent. of cases. A strongly positive Wassermann constantly present in several tests is generally regarded as almost absolute evidence of syphilis. If the dentist has Wassermann tests made on his patients it is important for him to know how to interpret the results, particularly negative results. Primary syphilis may not give a positive Wassermann for several weeks. Locomotor ataxia cases may have negative tests in 60 per cent. of cases. Cerebrospinal syphilis may show a negative test on the blood and a positive test on the cerebrospinal fluid together with an increase in the number of cells in the fluid (normally only about four cells per cubic millimeter).

Relation of Syphilis to Dental Practice.—In conclusion it may be stated that from the standpoint of the dentist, syphilis is one of the most important systemic diseases

bearing upon his work. The disease is so widespread and the oral manifestations so frequent, that the question of infection is always present. If a patient were just at the end of the secondary stage, the mucous patches just healed, there would be nothing characteristic to be seen in the mouth, yet the spirochetæ would abound, so that constant care is the only safeguard. Accidental infections are more frequent than is generally believed. When a professional man learns the nature of the sore on his finger, he never speaks of it. A few associates who happen to know of it never refer to his misfortune. His physician keeps his confidence, so the danger is never emphasized. Working in the mouth with an unprotected abrasion or fissure on the finger, which is constantly bathed in saliva, or guarding the patient's gum with the finger and puncturing it at times with a pointed instrument is reprehensible practice. Sterilization of instruments for the protection of the next patient should, of course, be routine technic.

ACTINOMYCOSIS.

Pathology.—Actinomycosis is a chronic infectious granuloma produced by the *Actinomyces bovis* or ray-fungus. It is quite well known as a disease of cattle under the name of lumpy jaw or wooden tongue. The disease is not frequent in man. The germ is a branched form belonging to the higher group of vegetable organisms or actinomyces and presents radiating threads with bulbous terminations (Fig. 53). These may be seen in the pus from the lesions of the disease as small yellow so-called sulphur granules and have been grown on culture media and successfully inoculated into animals. The infection gains entrance through the abrasions in the floor of the mouth or through the teeth. It is said that the organism has been demonstrated in the cavities of carious teeth. It may also be carried in with the food. It causes a reaction in the tissues similar to the other granulomata—a low-grade inflammation, moderate infiltration of leukocytes and later proliferation of connective tissue to a degree that causes considerable gross swelling.

It then breaks down and suppurates, leaving fistulous openings surrounded by an excessive amount of scar tissue.

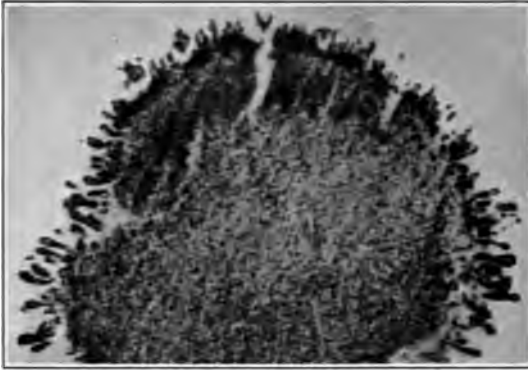


FIG. 53.—A typical "club"-bearing colony of actinomycetes. $\times 325$ diameters.
(From Wright.)

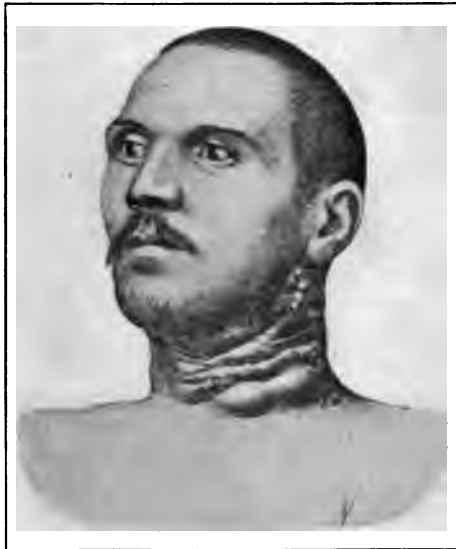


FIG. 54.—Actinomycosis of the neck.

Clinical Characteristics.—In man the condition usually comes on in the form of a chronic enlargement of the jaw quite like sarcoma, with which it was formerly confused. At first it may simulate alveolar abscess. If opened it leaves an obstinate suppurative condition about the lower jaw, with cellulitis of the neck. The tongue may show small growths (Fig. 54). The disease has a tendency to generalize as a chronic pyemia with metastatic abscesses in the bones in the liver, brain and other organs. There may also be a miliary actinomycosis similar to miliary tuberculosis. Intestinal and pulmonary actinomycosis are also well recognized forms and may be either primary or secondary to lesions elsewhere. The diagnosis is made on the yellow granules and the Gram-staining ray-fungus.

LEPROSY.

Nature and Distribution of the Disease.—Leprosy is a chronic infectious disease caused by the *Bacillus lepræ*, characterized by granulomatous nodules in the skin and mucous membranes and changes in the peripheral nerves leading to anesthesia of the affected areas. The dentist about to go to the Philippines, India or China should know that leprosy abounds in the Orient. There were estimated to be at least 100,000 cases in British India. There are a few hundred cases in the United States.

Pathology.—The bacillus of leprosy resembles the tubercle bacillus in that it is acid-fast but may be distinguished by the fact that it occurs in enormous numbers in the leprous nodule. It is very difficult to find the tubercle bacillus in skin lesions. The *lepra* bacillus is also more coarsely granular than the tubercle bacillus and occurs in bundles or palisades; never in chains. As a final test it cannot be inoculated into guinea-pigs successfully nor grown on artificial culture. The bacilli are given off from the open sores and are especially abundant in nasal secretions. They are present in the saliva when there are lesions in the mouth or throat. So far as is known the initial lesion is an ulcer above the cartilaginous part of the nasal septum. The disease takes *two*

forms at first—the nodular or tubercular leprosy and the anesthetic leprosy (Fig. 55). In the former there appear areas of hyperemia and swelling in the skin followed by



FIG. 55.—Anesthetic leprosy with mutilating results. (From a photograph of a leper in the Sandwich Islands. (Ormsby.)

sharply outlined nodules which on section show the organisms in large numbers in a granulomatous matrix. The mucous membranes of the eye, mouth and larynx may become

involved. The nodules are more vascular than tuberculosis or syphilis and consequently do not caseate but ulcerations result from secondary infections, trauma and the nipping of nerve fibers by the leprous infiltration under the skin. This latter process predominates in the anesthetic form. Trophic changes lead to contractions and necrosis and ultimately spontaneous painless amputation of fingers or toes. This form runs an extremely chronic course. The peripheral nerves show the granulomatous tissue and infiltration with round cells, but the bacilli only in small numbers. The lymph glands in both forms are enlarged and like the nodules show the bacilli in large numbers.

There is no evidence of hereditary transmission. Children of lepers removed at once to sanitary surroundings usually do not develop the disease. Transmission is apparently by quite intimate contact and probably sometimes by contaminated clothing.

GLANDERS.

Pathology.—Glanders is a specific infectious disease caused by the *Bacillus mallei*; rather common in horses and occasionally transmitted from them to man. The horse shows it as a foul ulceration of the nasal mucous membrane, or when affecting the superficial lymph glands and vessels as granulomatous nodules or buds under the skin. The latter is known as "farcy." The *Bacillus mallei* may be grown rapidly on ordinary culture media and shows a characteristic play of colors on potato. It is not acid-fast. Mallein, analogous to tuberculin and luetin is made from a killed culture and used for diagnostic purposes.

Human Glanders.—In man it is a very fatal disease acquired by contact with infected horses or receiving the *Bacillus mallei* on an abraded surface of skin or mucous membrane. The incubation period is only three or four days and acts like septicemia, which is the usual clinical diagnosis. The chronic form produces ulcers and subcutaneous nodules, which show the granulomatous structure, lymphoid and epithelioid cells and glanders bacilli. There are ulcers in

the nose and often laryngeal symptoms. Such cases are obviously infectious to dentists and others. Fortunately the cases are rare.

RARER FORMS OF GRANULOMATA.

Rhinoscleroma, mycetoma or madura foot and sporotrichosis are further examples of infectious granulomata, but they are rare and unimportant. Certain protozoa and also yeasts may induce the granulomatous tissue reaction, which is no more specific than simple inflammation. The latter shows variations, depending upon the particular causative agent. Similarly the granulomata show minor variations, but as a group are characterized by slow growth, chronic inflammation and connective tissue overgrowth. They may form lumps in gross appearance like true tumors, but pathologically have no relation to true tumors.

CHAPTER XIV.

TUMORS.

Nature of Tumors.—A true tumor or neoplasm consists of a lawless overgrowth of a tissue, an indefinite multiplication of the cells from which it springs. Instead of the cell growth proceeding toward normal structure, as for instance the cells of the deeper layers of the skin multiplying and flattening out to form the squamous cells of the surface of the skin, the tumor cell simply multiplies without regard for normal structure or function. Just what the directional or guiding influence is in normal cell growth, as exemplified, especially in embryological processes, is a mystery. The loss of this control over physiological cell growth or the cause of tumors is also a mystery. In the first stages of the embryo there is no differentiation of cells. All the cellular energy is used in cell division. Gradually functions are taken on and reproduction is less active. In the adult tissue the more highly differentiated or specialized the cells are, to perform certain functions, the more the reproductive function is repressed. For example, nerve cells have practically no power of regeneration. Connective tissue the least specialized has great power of regeneration. The tumor cell energy is used in cell division; its normal function such as glandular secretion is lost. It is a parasite on the surrounding tissue, upon which the tumor depends for its blood supply. So completely may the functional differentiation be subordinated to endless cell division that the blood supply may be mechanically squeezed out. Inflammations, infections, degenerations and necroses may be superimposed upon this neoplastic tissue just as a normal tissue would be involved, but the tumor formation is an absolutely distinct pathological process.

Theories of Etiology.—There are three main theories of the etiology of tumors:

1. *Cohnheim's theory of embryonic rests* or remnants. In the complex processes of development during embryonic life, groups of cells are believed to become detached and remain as separate nests and later, when for some reason conditions are more favorable, begin to grow as undifferentiated embryonal cells would grow. Many tumors appear along lines of fusion in embryological processes, such as the midline of the body and in the site of the primitive facial clefts. Regions where the embryological transformation has been most complex, such as the gill arches in the neck, are frequent sites of tumors. For example, the mixed tumor of the parotid usually shows islands of cartilage, which are probably derived from the primitive gill arches. Tumors arise from the branchial clefts. In certain cystic ovarian tumors, all kinds of structures such as teeth and hair are jumbled together without any semblance of order, so that one can hardly escape the idea that in some tumors at least, embryonal rests play a part.

2. *Chronic irritation*, mechanical, chemical or thermal. This is based on the frequent observation that tumors develop at the point of prolonged irritation. Cancer of the lower lip may appear at the point where a pipe, especially the hot clay pipe is habitually carried. Cancer of the tongue or cheek has often occurred opposite a jagged tooth, sometimes preceded by a traumatic ulcer or patch of leukoplakia. Warts or pigmented moles where rubbed by the collar may become cancerous. Sarcoma of bone occasionally results from trauma such as contusion. The irritation of ulcers in a variety of conditions lead to new growths; for example, ulcer of the stomach, ulcer in the gall-bladder from gall-stone, ulcer of the leg as from varicose veins, and laceration of the cervix of the uterus. The irritating effect of the x-ray may cause cancer and probably the prolonged application of caustics such as the "touching up" of sluggish sores with silver nitrate. Again one becomes convinced that irritation is a factor in certain tumors. It is probably only a predisposing cause, since many tumors occur where there

is no recognizable irritation. It would be difficult, however, to exclude chemical irritants, such as the poisons of metabolic disorders or the toxins of chronic infections.

3. *Parasitic Theory*.—A number of times a microörganism, either vegetable or protozoan, has been announced as the specific cause of cancer, but none of them has stood the test of time and further research. Cultures of the suspected organism were uncertain and did not reproduce tumors. In mice and rats, implanted nests of cells will grow just as a metastatic or secondary tumor, but this can be explained by the great tendency of cancer cells to multiply and grow in an abnormal environment. The parasitic theory is now quite generally discarded, although by no means disproved.

Other theories of tumor formation, such as hereditary and nervous influences, are too vague to deserve further consideration. Extensive research is being carried on in connection with the problem of new growths and more definite information may be gained in the near future. Cancer is apparently on the increase during recent decades. Some investigators have attributed it to syphilis and the more general use of tobacco and alcohol. Cancer in the mouth particularly may have these factors as predisposing causes.

Benign and Malignant Tumors.—Tumors are divided into two broad groups—benign and malignant. The quality of malignancy, however, if not present from the beginning is potentially present in all tumors, so that a malignant change may take place during the course of benign neoplasms. The tendency to undergo this malignant change varies widely in different types of benign tumors from almost none, as in the case of fatty tumors (lipoma), to so marked a degree as in tumors of the breast, that removal is the only escape from the constant suspicion of malignant disease.

Malignant Tumors.—The characteristics of malignancy are: (1) *Invasion* of surrounding structures by the tumor cells. By mechanical pressure due to the lawless cell growth and by a chemical cytolytic action, the malignant tumor extends directly into adjacent tissues, whether bone or nerve or bloodvessel. In a gland (acinus) the first tendency to

invasion may be recognized by the cells breaking through the basement membrane, which normally so perfectly controls the epithelial growth. (2) *Metastasis*, or the lodging and growth of malignant tumor cells detached from the primary growth in other parts of the body. The cells are able to survive in foreign soil because, as stated before, all their vital energy is directed toward growth and reproduction. They may be carried either in the lymph or blood circulation. The former is more frequent in tumors of epithelial tissue. Consequently involvement of regional lymph glands is more characteristic of epithelial than of connective-tissue growths. Metastatic or secondary tumors sometimes exceed the parent growth in size. Sometimes they are so numerous that the internal organs are riddled and with a distribution similar to that of miliary tuberculosis. (3) *Cachexia* results from malignancy. It includes the emaciation, anemia and exhaustion of a patient with these growths. It is due to toxins elaborated in some way in connection with the abnormal cell growth. Sometimes the cachexia is apparent quite early, before the tumor is large enough to cause any symptoms mechanically or any local interference of function. These three are the essential characteristics of malignancy. There are other features really implied in the foregoing which are of practical value. *Rapid growth* of the malignant tumor in comparison to that of the benign tumor results from the subordination of all cell function to cell division. A benign tumor may remain the same size for years; a malignant one steadily enlarges. *Mitotic figures* in the cells as evidence of active cell division serve also as a diagnostic aid.

Fixation of a growth to the surrounding parts is due to invasion. A benign tumor is freely movable on the underlying parts and the skin freely movable over it unless it originates in the skin. *Pain* also results from the invasion and irritation of nerve fibers. Lancinating pains in cancer of the tongue are frequent. *Excessive vascularity* is necessary in the rapid growth of malignant tumors. A network of veins in the skin overlying such a tumor is clinical evidence of its nature. Of course, stasis from mechanical obstruction of the local circulation would have to be excluded.

Hemorrhages from a growth due to this congestion or later due to erosion of a bloodvessel of some size as well as a ready tendency to oozing on light manipulation are further clinical signs of malignancy. *Tendency to recurrence* after removal is the great tendency to proliferation of a few residual cells, which may have migrated slightly beyond the gross limits of the tumor. *Absence of any limiting capsule* is seen in malignant tumors. The definite capsule of benign tumors often permits of their being easily shelled out. If the benign tumor undergoes subsequent malignant change it invades through the capsule at some point. *Retraction of overlying skin*, such as the nipple in cancer of the female breast is due to involvement of vertical trabeculae of connective tissue. *Tendency to central degeneration* results from pressure of surrounding parts and a growth so rapid that the blood supply cannot keep pace with it. Atrophy and necrosis are frequent. In growths of the skin and mucous membrane, the surface cells are farthest from their blood supply as well as being subject to trauma and infection, so that *ulceration* results. Benign tumors rarely ulcerate unless subjected to considerable injury. As said before, tumor tissue is exposed to the same etiological agents and subject to the same pathological processes as normal tissues.

Benign Tumors.—Benign tumors produce symptoms mainly by mechanical pressure on adjacent structures. Tumors of the teeth or dental follicles cause deformities or press on nerves and cause pain. Tumors in the neck press on the trachea or bloodvessels or nerves. Tumors of the pelvis may obstruct the ureter or bowel. Tumors of the spinal cord may destroy nerve tracts purely by pressure and cause paralysis. Then there is always the possibility of malignant change, or as it is sometimes inaccurately termed, malignant degeneration.

Metaplasia.—Tumors also furnish frequent examples of the process of metaplasia—that is, the transformation from one type of tissue to another type, such as from connective tissue to bone, cartilage or mucoïd tissue. In the reversion of the tumor cells to the embryonic type, development may proceed again without any physiological control. As a result sometimes finds in sections of tumors islands of cartilage

scattered indiscriminately with mucoid tissue, bone and any kind of connective tissue.

The classification of tumors is not very satisfactory and probably cannot be until the etiology is better understood. Tumors of connective-tissue origin (fibromata) behave differently from those of epithelial origin (epitheliomata), so that this may be made the basis of the first subdivision. The ending "oma" means tumor.

CLASSIFICATION OF TUMORS.

A. Connective tissue and other non-epithelial tumors.

(a) Benign.

Fibroma.

Myoma.

Lipoma.

Myxoma.

Chondroma.

Osteoma.

Angioma.

Keloid.

Glioma.

Mixed tumors as of parotid—terminology.

(b) Malignant.

Sarcoma—small round cell, large round cell, spindle cell, mixed cell, giant cell, epulis.

Lymphosarcoma.

Endothelioma.

Melanoma.

B. Epithelial tumors.

(a) Benign.

Papilloma.

Odontoma.

Adenoma.

Dermoids.

(b) Malignant.

Carcinoma.

Epithelioma—rodent ulcer, x-ray cancer.

Adenocarcinoma.

Medullary.

Scirrhus.

C. Cysts.

Retention cysts.

Dentigerous cysts.

Tubulo cysts.

Liquefaction cysts.

Dermoid cyst.

Cystoma.

D. Teratomata.

BENIGN TUMORS OF NON-EPITHELIAL ORIGIN.

Fibroma.—Fibroma is a benign tumor of fibrous connective tissue. As the latter abounds everywhere fibromata have a wide distribution. They may occur anywhere. However, it will be noticed that tumors have habitats where they occur in the great majority of cases. They occur in certain types of patients and under certain conditions. All these factors make up the practical knowledge of tumors. Fibromata occur in the skin and mucous membranes as small pedunculated growths or as sessile masses. Pure fibromata are not very common. Usually there is a combination with another tissue, such as mucoid tissue in the nasal polyp. Such mixed tumors are designated by the proper prefixes, as fibromyxoma. Fibrous fatty tumors (fibrolipomata) are very frequent in the subcutaneous tissues. Fibromata and fibromyoma are the commonest benign tumors of the uterus. A particular form of fibroma of interest to the dentist arises from alveolar periosteum, especially opposite a carious tooth. Any tumor arising at this point is called an epulis, the term meaning "upon the jaw." Some of these growths, however, have a low grade of malignancy (giant-cell sarcoma), as will be described later, so that the term epulis is ambiguous. Some writers use it for the benign form, others for the malignant form. Fibromata are sometimes divided into *hard* and *soft* varieties, referring directly to their consistency (Figs. 56, 57 and 58). The hard ones are slower growing and denser because the fibrous tissue has reached a more adult form. The strands of fibrous tissue may be seen running in all directions in cut sections. The soft fibromata are

more cellular, more rapidly growing and for that reason have a greater tendency to malignant change.



FIG. 56.—Fibroma of uterus. (Low power.) (Park.)



FIG. 57.—Fibro-adenoma of breast. (Low power.) (Park.)

Myoma.—Myoma is a benign tumor of muscle tissue (Fig. 59). It may be of two kinds: *Leiomyoma* involving the

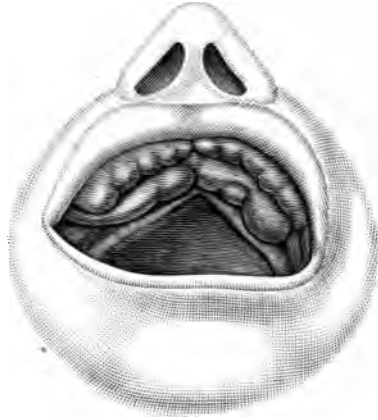


FIG. 58.—Lobulated fibroma of the gums from irritation of a dental plate.
(von Bergmann.)



FIG. 59.—Section of portion of a pure myoma, showing the character of the nuclei and the appearance of the cells cut longitudinally and transversely (Perls.)

unstripped muscle or *rhabdomyoma* involving the striped muscle. The latter is rare. Ninety-nine per cent. of myomata are of the involuntary muscle tissue. They

occur mainly in the uterus and intestine, occasionally in the skin. In the gross they are of rather firm consistency and grayish in color. Microscopically the muscle fasciculi can be seen running in all directions as in fibroma, but the nuclei of the muscle fibers are elongated rods often with a regular parallel arrangement. The nuclei of fibrous tissue are irregularly spindle-shaped. In cross-section muscle fibers show some cytoplasm while the fibrous strands are "naked." Some connective-tissue stroma is present in all myomata and as the tumor grows older there is a "fibroid degeneration" of muscle tissue. There are also frequently other forms of degeneration in the center of myomata or fibromyomata which often attain considerable size, so that the blood supply is inadequate for normal nutrition. Hyaline degeneration and calcification occur—even necrosis and cavity formation. This applies mainly to "uterine fibroids" which are very common tumors. The main symptom is excessive menstruation (menorrhagia) or even prolonged bleeding (metrorrhagia), which may cause the severest grades of anemia. A number of pelvic conditions may cause this form of hemorrhage and secondary anemia. The dentist, therefore, should not jump at the conclusion that anemia in a woman otherwise healthy and well nourished is due to oral sepsis. Virulent hemolytic streptococcus tooth infections may produce the same degree of anemia, but it is only one of a large number of causes. A very anemic patient should always have a general examination before extensive extractions are carried out. *Rhabdomyoma* is composed of striated muscle, but in the reversion to the embryonic type of cell the striation is often lost or partially lost and the cells poorly differentiated. These rare tumors may occur in the heart muscle or in the skeletal muscles, and at times arise from embryonic rests in locations where there normally is no muscle at all.

Lipoma.—Lipoma or fatty tumor is perhaps the commonest subcutaneous tumor. It may occur also in the intestine and retroperitoneally and rarely in the intermuscular spaces. Around the neck and shoulders and down the back lipomata may frequently be found. They are soft in consistency and

lumpy due to the lobulated structure. The trabeculae extend up to the skin so that a lipoma on being picked up between the fingers puckers the overlying skin. They are freely movable under the skin and on the underlying structures. Occasionally they occur symmetrically on both arms and legs



FIG. 60.—Diffuse symmetrical lipoma, multiple. (Lexer.)

(Fig. 60), sometimes a number of them, presenting the condition known as "symmetrical lipomatosis." A large lipoma encircling the neck forms the so-called "fatty collar." Sometimes lipomata are so soft and fluctuant that they may be mistaken for fluid, such as a cold abscess. The fat may be of somewhat different consistency and color from that of

the surrounding tissues. It is also quite independent of the general physiology in that it remains unabsorbed if the whole body is emaciated. There is almost no tendency to malignant change, although there may be metaplastic changes such as to mucoid tissue or islands of bone. They are objectionable mostly on account of unsightliness and pressure symptoms. Occasionally they attain enormous size. Fibrolipomata may be quite firm in consistency.

Myxoma.—Myxoma is a tumor of mucous connective tissue, and as such is quite closely related to a soft fibroma. True myxomata, however, contain mucin, which may be identified chemically and stained differentially (with thionin)

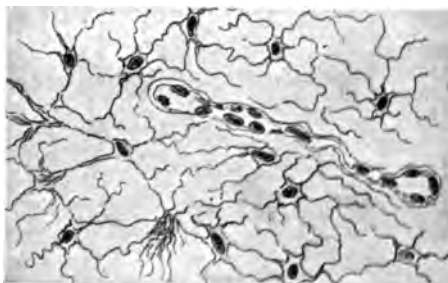


FIG. 61.—Section from typical portion of a mucoid polyp. (Collection of Royal Victoria Hospital.)

in sections. Mucoid tissue does not exist in the adult body, but makes up the Wharton's jelly of the umbilical cord, so that myxoma again illustrates the reversion to the embryonic type of cell in tumors. The gelatinous matrix of mucoid tissue is interspersed with stellate cells with long processes of the so-called spider cells (Fig. 61). Some nasal polyps are myxomata or fibromyxomata. They obstruct nasal breathing and interfere with drainage and may produce deformities of the face and chest similar to those of adenoids. In fact, the two conditions are often associated. The pinched nose, the high, narrow palatal arch of obstruction to nasal respiration and the associated history of mouth breathing and snoring at night should be familiar to the dentist. Adenoids are

due to hyperplasia of lymphoid tissue just as enlarged tonsils. Polyps may entirely fill the frontal and maxillary sinuses. By pressure in the latter, symptoms referable to the upper teeth may be produced. Myxomatous "degeneration" (really metaplasia) is frequent in many tumors.

Chondroma.—Chondroma is a tumor of cartilage of any form. It may originate as a protuberant outgrowth from normally placed cartilage, such as the articular cartilages of the fingers forming the so-called *ecchondroma*; or it may



FIG. 62.—Chondroma.

arise in regions where there is no cartilage normally either from "cell rests" or by metaplasia from other mesoblastic tissues. This form is known as *enchondroma*. Hyaline cartilage is the most common variety found. Chondromata are apt to develop in early life and have often been associated with or preceded by rickets, in which there is an overgrowth of cartilage leading to epiphyseal enlargement and projections of cartilage into the shaft of bone. As in normal cartilage, the blood supply of these tumors is very scant, so that secondary degenerations may occur and any processes of

repair are very sluggish. On the other hand chondromata have the peculiar feature of giving rise at times to benign metastases. Detached islands of cells (Fig. 62), chondroblasts with vegetative activities almost entirely may develop nodules of cartilage with no other characteristics of malignancy. They have only a slight tendency to undergo true malignant change (Fig. 63).



FIG. 63.—Sarcoma of the superior maxilla. (Hertzler.)

Osteoma.—Osteoma is a benign tumor of bone. It has the architecture of bone with Haversian systems. It usually arises in relation to normal bone, forming a protuberant mass quite distinct from simple exostosis which is a hyperplasia in response to the stimulus of overuse or inflammation. Osteoma arises independently of any physiological cause. Exostosis results at muscular insertions in proportion to the

strength of muscle action. The coronoid process of the mandible, and the keeled sternum of birds are formed in this way. Osteoma occurs on the mandible, usually near the chin and in the maxilla, also in the skull where it sometimes (Fig. 64) causes symptoms by pressure in the brain or cranial nerves. Osteoma of the orbit is not so uncommon. The eyeball is necessarily pushed forward (unilateral exophthal-



FIG. 64.—Osteoma of the supra-orbital sinus. The roof of the orbit has been perforated and an irregular nodule thrust within the orbit. (Hertzsler.)

mus). Osteoma may also arise primarily in cartilage or even fibrous tissue. There may also be a metaplastic ossification secondarily in other tumors. Calcification is only the deposition of lime salts without bony structure. Osteoma may be of ivory hardness—the so-called eburnated osteoma or osteoma durum. In contrast it may arise from cancellous bone and be spongy in structure—osteoma spongiosum.

Odontoma.—Odontoma is a tumor of tooth tissue, arising from the germs of teeth or from developing teeth (Fig. 65). A tooth has a rather complex embryological development. The enamel organ is a downward protrusion of the surface epithelium of the mouth, beginning as early as the end of the second month of fetal life. Then the dentin papilla forms

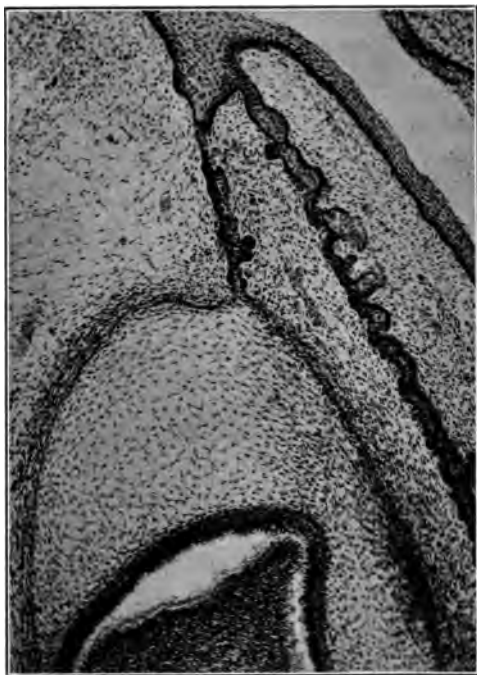


FIG. 65.—Developing tooth.

in the mesodermic tissues beneath the enamel organ. A third separate process later forms the root papilla, supplying vessels, nerve and pulp. Anyone of these three developmental processes may leave detached rests of cells, which may later form tumors. Sometimes the tumors show growths from all three of the primitive tooth

a conglomerate or composite mass. Hence the tumors of teeth may be classified as follows:

1. Tumors from enamel organ—epithelial odontoma or adamantinoma.

2. Tumors from the dental capsule and its contents. A variety of forms results from the preponderance of the different tissues: Follicular odontoma or dentigerous cyst, fibrous odontoma and cementoma.

3. Tumors from the root papilla—radicular odontomata.

4. Tumors from the whole tooth germ—composite odontomata.

Epithelial odontomata cannot properly be considered under "tumors of connective tissue." They originate from the epithelial enamel organ and histologically have the structure of epithelial alveoli and contain dark mucoid fluid. However, they have fibrous septa, which may even be ossified.



FIG. 66.—Dentigerous cyst.

Follicular odontoma or dentigerous cyst is so-called because the dental capsule remains intact, its walls become hypertrophied and the tooth retained in various stages of preservation. It may be a supernumerary tooth. These tumors are more common in the lower jaw and may attain considerable size, spreading the two walls of the mandible apart and extending lengthwise sometimes nearly the whole length of the bone (Fig. 66). There may be an ounce of more of viscid fluid in the cyst. Obviously such a swelling of the jaw would bring up a number of diagnostic possibilities, especially osteoma, sarcoma, osteomyelitis, or abscess, syphilis and actinomycosis.

Fibrous odontoma is really a fibroma of the dental capsule with small remnants of a tooth in the center. It is of interest because it has been found associated quite frequently with rickets. It is suggestive of the cause of delayed dentition and malformed teeth in that disease. These fibrous odontomata are also frequently multiple.

Cementoma shows a thickened ossified capsule with the structure of cementum and a tooth embedded in the center. Irregular cavities in the bony structure are characteristic of this form of odontoma.



FIG. 67.—Odontoma of lower jaw. (von Bergmann.)

Radicular odontoma arises from the root structures after the tooth proper has been fully formed. These root structures probably develop mostly after birth. Obviously there can be no enamel in them. They consist of cementum, dentin and a nucleus of calcified pulp.

Composite odontoma results from an intermingling of the primitive tooth buds quite early and often of several teeth. These growths present a conglomeration of all the tooth elements. They usually occur in the mandible but may occur and attain large size in the maxilla and involve the antrum (Fig. 67).

Angioma.—Angioma is a tumor made up of vessels—bloodvessels in *hemangioma*, lymph vessels in *lymphangioma*. Many so-called angiomata are merely tufts of dilated vessels or telangiectases. However, there are true tumors of vessels with actual proliferation of capillaries, and especially an overgrowth of the endothelial cells, which are large, rounded and often more than one cell deep. Birthmarks or nevi are angiomata usually. They may be bright red



FIG. 68.—Angioma of the face.

from arterial blood or deep blue from large venous channels. Very large sinuses in these tumors are the special feature of *cavernous angioma* or cavernoma (Figs. 69, 70 and 71). Nevi are frequently present at birth. They sometimes disappear spontaneously or they may steadily enlarge and should be destroyed or removed. They usually have a distinct afferent artery and efferent veins. Hemangiomata occur on the skin of the face and form a disfiguring mass of thinly covered bloodvessels. They occur also in the tongue

and sometimes bleed profusely. Lymphangiomata also occur in the lips and tongue and produce unsightly excres-

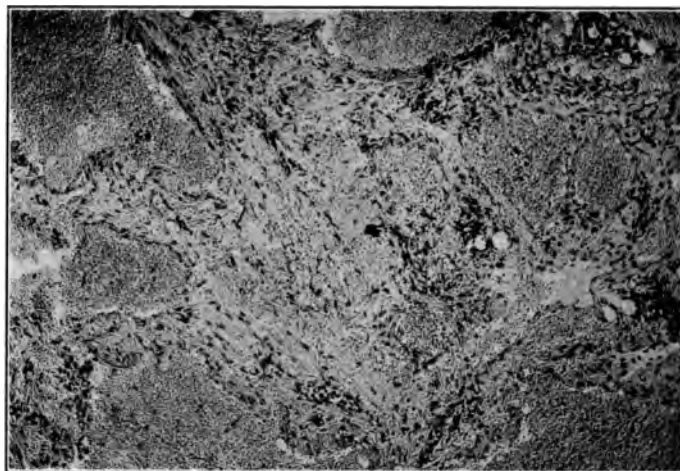


FIG. 69.—Cavernous angioma.

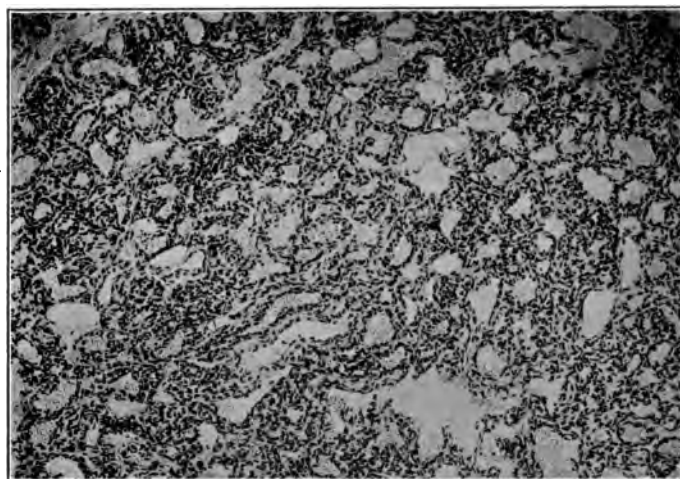


FIG. 70.—Vascular nevus.



FIG. 71.—Benign nevus.



FIG. 72.—Lymphangioma of lip; macrocheilia. (Neisser.)

cences (Fig. 72). The tongue may be so large as to be forced out of the mouth (lymphangiomatous macroglossia). These cases are subject to curious attacks of acute inflammation. There may also be cavernous lymphangioma. Very large cystic accumulations of lymph are known as hygroma. They occur as tense cystic tumors in the neck but are not common.



FIG. 73.—Keloid. (Park.)

Keloid.—Keloid is a tumor of fibrous tissue occurring in a scar. It is on the border-line between a hyperplasia of fibrous tissue and a true fibroma. Scars of surgical incisions—the connective tissue of sinuses, as of scrofula or a vaccination scar or some very trivial skin injury may cause them. Certain individuals have a definite tendency to keloid for-

mation. The colored race are particularly subject to them (Fig. 73).

Glioma.—Glioma is a tumor of the neuroglia of nervous tissue, usually the white matter of the brain or cord. They are of importance because of the serious pressure symptoms they may produce intracranially or intraspinally.



FIG. 74.—Multiple fibromatoid overgrowths along the course of the cutaneous nerves. (Herczel.)

Neuroma.—Neuroma as a growth of nerve cells—the most highly differentiated cells in the body practically never occurs. So-called false neuroma or neurofibroma occurs not infrequently on the peripheral nerves. Often they are multiple, forming hundreds of small flat or pedunculated

tumors in the skin supplied by a certain nerve. Sometimes they occur all over the body, a few of them reaching great size. This is called generalized neurofibromatosis or von Recklinghausen's disease (Fig. 74). Sections of excised nodules show nests of nerve fibers in a mass of fibromatous tissue.



FIG. 75.—Mixed tumor of the parotid, showing endothelial areas undergoing active proliferation. (Hertzer.)

Mixed Tumors.—Mixed tumors consisting of a great variety of different kinds of tissue occur and usually in certain locations, especially the salivary glands and the kidney. These are regions of complex embryological transformation. The parotid is in relation to the primitive gill arches and gill

clefts, so that "rests" of cells destined to form cartilage, and any kind of mesodermic structures and even epithelium may be included in the development of the parotid gland (Fig. 75). The mixed tumors of the parotid may contain all these tissues irregularly distributed throughout their substance (Fig. 76). There may also be an endothelial origin for some of them. The tumors may be congenital,



FIG. 76.—Mixed tumor of parotid.

but usually appear in early adult life. They are benign, but may after many years take on malignant change (Fig. 77). They are encapsulated, but nodular and irregular and may involve the facial nerve. Deep tumors may grow toward the pharynx. Usually these parotid growths attain the size of an egg or a lemon and remain stationary for years. At times, however, they grow steadily to enormous dimensions, equalling the whole head in size. Central cystic

degenerations are then frequent. Mixed tumors of the other salivary glands are less frequent.

The kidney develops from the primitive body segments or myotomes, which also go to form the structures of the body wall in that region. Accordingly, one finds muscle, fibrous tissue, elastic tissue cartilage and fat, as well as remnants of the kidney tubules. These tumors are usually malignant.

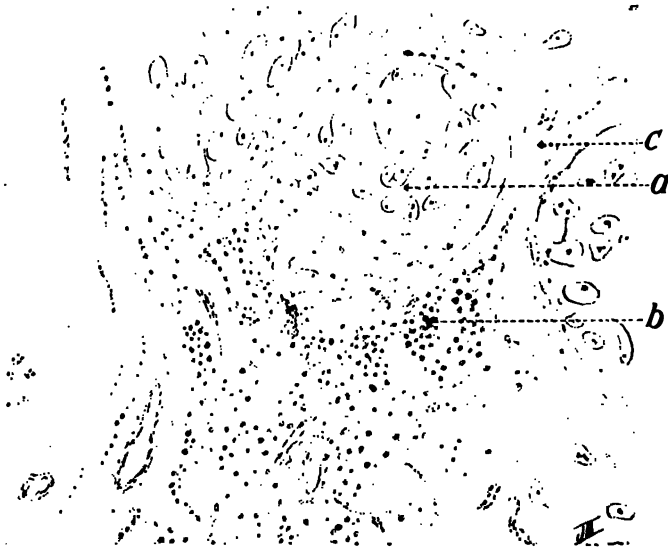


FIG. 77.—Chondrosarcoma (mixed tumor) of testicle: *a*, area of cartilage; *b*, sarcoma cells; *c*, connective tissue. (Hertzler.)

Terminology of Tumors.—In the terminology of these mixed tumors, prefixes are used to indicate the various types of tissues found on pathological examination. The main term to which the “oma” is added indicates the predominant tissue in the tumor. For example, a mixed tumor of the parotid might be a fibro-myxo-lipo-osteo-chondroma. Here cartilage would predominate with the other tissues present in varying amount. When connective-tissue tumors are

malignant or become malignant, they are called sarcoma. If the above tumor should undergo malignant change, its technical pathological name would be fibro-myxo-lipo-osteochondro-sarcoma. The mixed tumors of the kidney are frequently fibro-lipo-myosarcoma.

MALIGNANT TUMORS OF NON-EPITHELIAL ORIGIN.

Sarcoma.—Malignant tumors of connective tissue, the sarcomata, have certain group characteristics. The cells resemble the embryonal connective-tissue cells to a degree that is proportionate to the malignancy of the tumor. The degree of reversion to the undifferentiated type of cell determines in large measure the rate of growth and the degree of malignancy. Sarcomata are richly cellular, but have a characteristic interstitial substance which may be fibrillary or granular. Bloodvessels, especially in the soft, rapidly growing sarcomata, are imperfectly formed; at times the endothelial wall is entirely lacking, so that tumor cells come in direct contact with the blood stream, consequently cells may readily be brushed off into the blood stream. Metastases in sarcoma indicate that they are usually carried in the blood stream. They are frequent in the lung and at remote points from the original growth. Metastasis may occur, however, along lymph channels. Squeezing or forcible manipulation of any malignant tumors is objectionable, because of the danger of detaching cells that will form metastases. Sarcomata may arise in any part of the body and are frequently connected with bone. In gross appearance they vary from a grayish so-called "fish flesh" appearance to a pink color in the more vascular forms. They occur usually in the first half of life, often in infancy in contrast to the carcinomata which occur in the second half of life, usually between forty and sixty years of age.

Classification of the Sarcomata.—Sarcomata may be subdivided according to the predominating type of cell as follows:

Small round-cell sarcoma, in which the cells are small from rapid division, are quite undifferentiated and have a mini-

num of intercellular substance. The nuclei are large and show frequent mitotic figures (Fig. 78). This all implies the highest degree of malignancy. The growth invades in finger-like processes into the surrounding tissues. Widespread metastasis rapidly occurs and early death. This form may originate in the jaws or antrum.

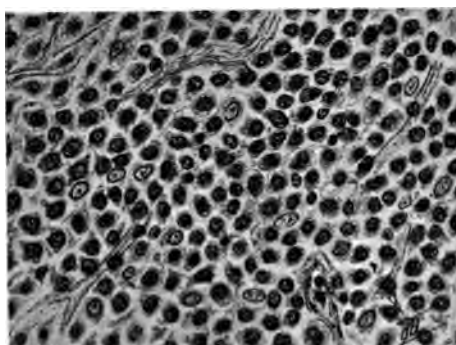


FIG. 78.—Small round-celled sarcoma. (Hertzsler.)

Large round-cell sarcoma is a slower-growing, less-malignant tumor than the small cell type. The cells are larger, have more cytoplasm and an intercellular reticulum. Some cells will show beginning differentiation by an oval or elongated shape. In the gross, this form is of firmer consistency and less vascular, than the small-cell sarcoma.

Spindle-cell sarcoma represents the next degree of cellular differentiation. The spindle cells often show slight fiber formation as well as various sizes and shapes. There may be considerable intercellular material giving the tumor a very firm consistency. This is the most frequent form of sarcoma. Metastases do not occur early and if the growth is thoroughly removed, there may be no recurrence.

Mixed-cell sarcoma is a name applied to mixed or intermediate types. The character of the growth is determined by the predominating cell (Fig. 80).

Giant-cell sarcoma is the least malignant form of sarcoma, and is most apt to occur in bones, especially from the interior,

but also from the periosteum. The large multinucleated giant cells are distributed through a sarcomatous matrix,



FIG. 79.—Spindle-cell sarcoma.

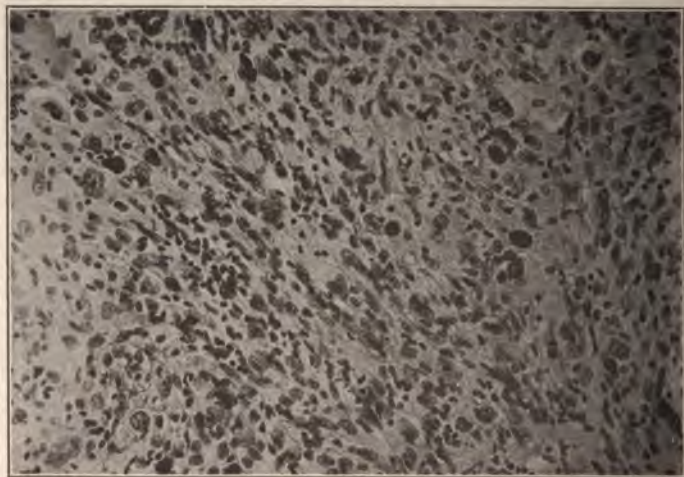


FIG. 80.—Mixed-cell sarcoma.

in which the spindle cell usually predominates (Fig. 81). Epulis may be a giant-cell sarcoma. The term would be

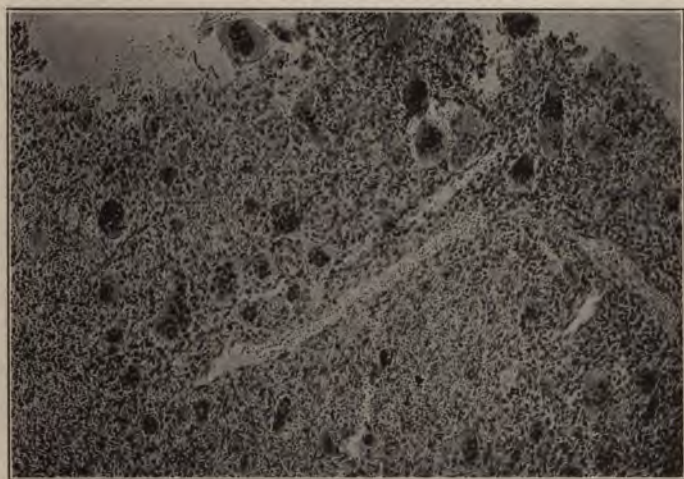


FIG. 81.—Giant-cell sarcoma.

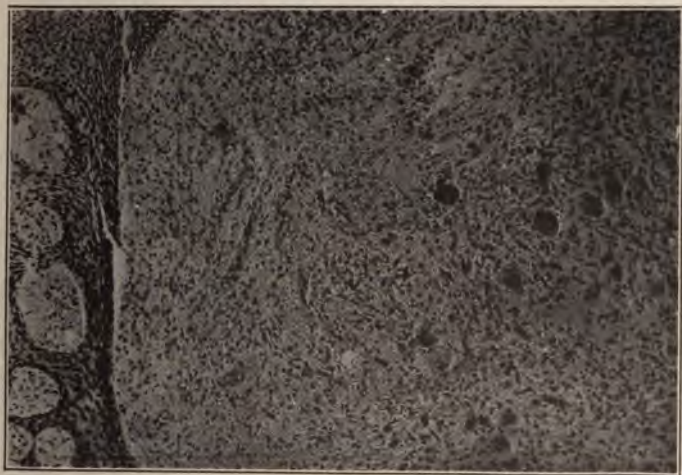


FIG. 82.—Epulis.

more distinctive if it were limited to this form, arising from the alveolar periosteum. As stated before, however, the term epulis is applied to any tumor on the gum, even inflammatory overgrowths. The giant-cell sarcoma form of epulis practically never metastasizes but it may extend locally and recur if the alveolar periosteum from which it arises as a pedunculated tumor is not thoroughly removed.



FIG. 83.—Periosteal sarcoma of the lower jaw. (Hertzier.)

Types of Sarcoma of Bone.—Sarcoma of bone of whatever cell type usually arises from the periosteum or the endosteum. The former, periosteal sarcoma is the more frequent. It forms an oval mass on the surface of the bone and may spread a considerable distance along the periosteum. For example, periosteal sarcoma of the knee, involving the lower end of the femur, may extend up the shaft in finger-like processes so far that only hip-joint amputation gives

any hope of radical removal (Fig. 83). The shaft of bone is also invaded and causes absorption as shown in characteristic fashion in the x-ray plate. The invasion and rarefaction of bone is a differential point in the x-ray picture of periosteal sarcoma as distinguished from the periosteal thickening of syphilis. Endosteal, or central sarcoma, invades outward, thinning out the shaft of bone; finally to a degree that the "egg-shell crackle" can be felt on palpation. Spontaneous fracture may also occur, sometimes as the first symptom of these sarcomata. Bone sarcomata, in general, are quite vascular and show frequent hemorrhages and necroses within the tumor.

Multiple Myeloma (Synonyms—*Myeloma multiplex*, *Myelomatosis*, *Myeloid Sarcoma*) is a peculiar rare form of tumor of the bone-marrow, arising at multiple points simultaneously and in bones widely separated. It does not involve the osteogenic cells and shows no giant cells in its structure, but is derived from blood-forming cells of the bone-marrow, the myeloblasts and lymphoblasts. The bone-marrow is a complex tissue and it is seen that the bone-forming and blood-forming elements are quite distinct. Multiple myeloma has the peculiarity of growing locally and expanding the bone, producing palpable lumps, and even causing spontaneous fracture and yet does not give rise to metastases. Its local malignancy is of low grade, but the tumor mass will ultimately break through the shell of bone and invade the overlying tissues. The disease is always fatal in the end, which is usually within five years. These tumors usually occur in the sternum, rib, skull and at times the vertebrae and long bones. Only the red bone-marrow is involved and the blood-forming function is greatly impaired. A severe grade of anemia clinically like pernicious anemia results. Finally, the myelopathic albumosuria so characteristic of this condition is the presence in the urine of a substance known as Bence-Jones albumose, which precipitates out of the urine on slight heating, redissolves at boiling temperature and again precipitates on cooling. It occurs in nearly half of the cases.

The term myeloma is also used broadly to mean

tumor of the bone-marrow, including the giant-cell sarcoma arising from the osteogenic cells, which as stated, are independent of the blood-forming cells. The term myeloid sarcoma is best confined to this giant-cell form.

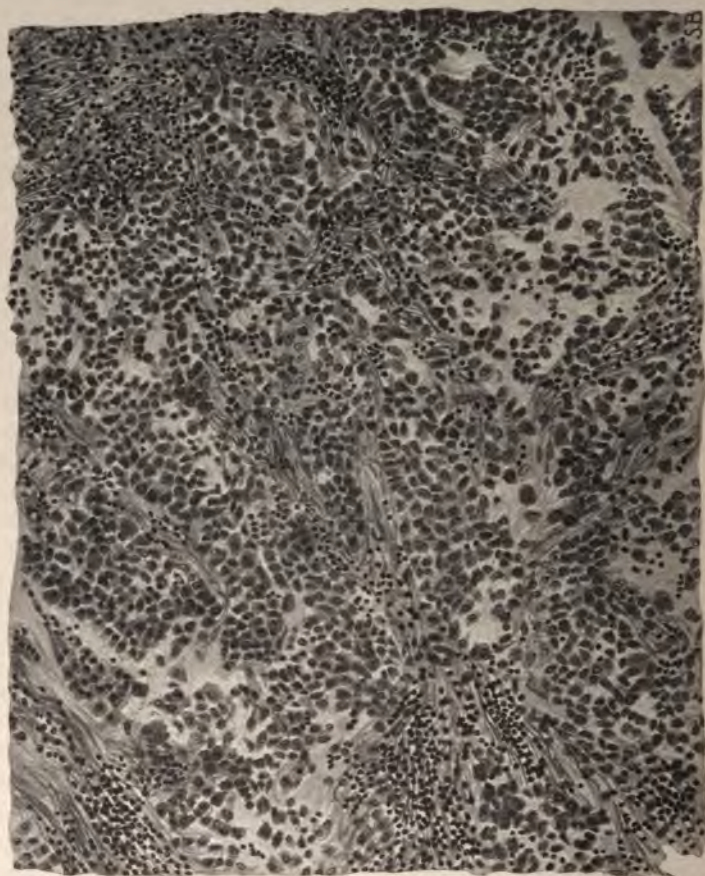


FIG. 84.—Lymphosarcoma of the neck. (Hertzler.)

Sarcoma of Lymph Glands.—*Lymphosarcoma* is a primary sarcoma of lymphoid tissue, usually the lymph glands

(Fig. 84). Superficially it resembles small round-cell sarcoma but differs radically in that the round cells of lymphosarcoma are at or near the adult state and relatively slow growing while the cells of small round-cell sarcoma have reverted to the embryonic state and are rapidly growing and of the most malignant character. Structurally too, there are differences. The reticulum of the lymph glands is seen in lymphosarcoma as well as vestiges of the germinal centers. Small round-cell sarcoma is just a dense mass of round cells. It may be secondary in the lymph glands or even arise from the connective-tissue elements of the lymph gland. Lymphosarcoma may for a long time be local and slow growing, but ultimately invades through the gland capsule into surrounding structures. It occurs in the lymph glands of the neck, where it must be differentiated from tuberculosis of the cervical lymph glands which is the commonest glandular enlargement in the neck and also from *Hodgkin's disease*. The latter causes a similar chronic enlargement of the lymph glands and is not very well understood but is now believed to be due to a chronic infection. A diphtheroid bacillus has been grown from the glands, but has not been established as the cause of the disease. Many lymph glands are involved and they are discrete, never matted together. Pathologically, the glands show marked fibrous and endothelial overgrowth and many eosinophiles. Both Hodgkin's disease and lymphosarcoma produce large glandular masses which may cause serious pressure symptoms in the neck and thorax and ultimately prove fatal. Early operation is important in these conditions and the dentist should be suspicious of them as soon as lymph-gland enlargement is out of proportion to conditions in the mouth. Involvement of another set of glands, such as the axillary or femoral as well as the neck glands, obviously distinguishes the condition from simple mouth infection.

Melanotic Sarcoma or Melanoma is a special form of sarcoma, characterized by the deposit of pigment (melanin) and by extreme malignancy. They usually originate in a pigmented tissue, especially the pigmented and hair

of the skin, also pigmented growths from the mucous membranes and from the choroid of the eye. There is some doubt as to whether the pigment cells in skin moles originate in the connective-tissue center or from the epithelial cells near the surface—in other words, whether the growth is a sarcoma or an epithelioma. It may be different in different cases. The term melanoma does not indicate either origin, but is definite in that it means a well-known clinical form of malignant tumor. Metastasis occurs as in sarcoma, that

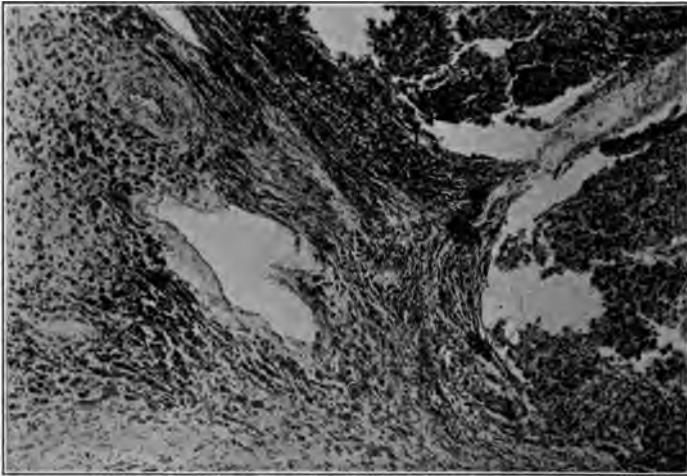


FIG. 85.—Melanotic sarcoma.

is, by the blood to distant parts, especially the liver and lungs (Fig. 85). Metastatic or secondary tumors may form in enormous numbers and with extraordinary rapidity. They may be many times larger than the original growth. The color varies greatly, usually quite dark and may be pure black. Some of the secondary tumors may show no pigment. Microscopically the cells may be of any type and are often divided into alveoli by septa of connective tissue. This arrangement is sometimes dignified by the special name of *alveolar sarcoma* (Fig. 86). The pigment may be

intra- or extracellular. A rapidly fatal melanoma occasionally develops in the ordinary pigmented skin mole, and

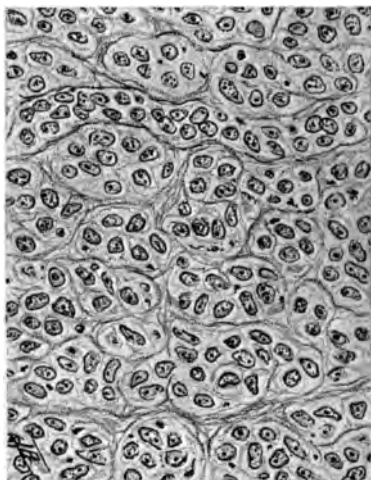


FIG. 86.—Alveolar sarcoma. (Hertzler.)

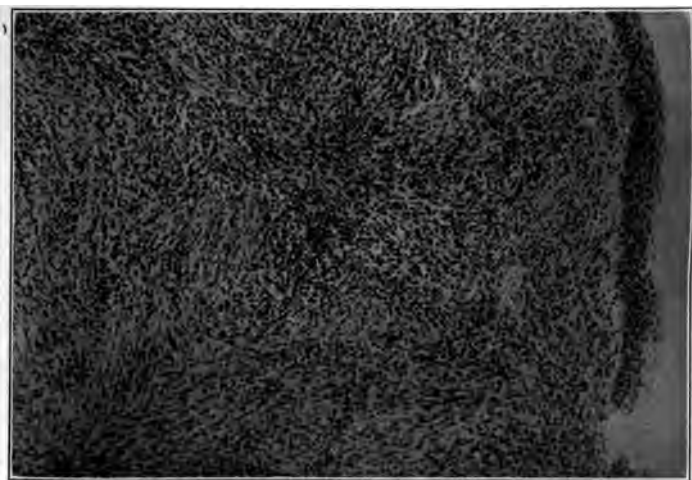


FIG. 87.—Fibrosarcoma.

especially one at a place which is constantly rubbed and irritated as at the back of the neck under the collar or in the axilla. The percentage of moles that become malignant is very small, but these growths are so frequent that death from a rapidly disseminated melanoma with extreme cachexia is not a very rare picture. Once the malignant change is apparent externally, as by ulceration and growth in a pigmented mole, it is often too late. Excision should be carried out, but some cells may have escaped. The dentist should, therefore, not encourage his patient in thinking that the pigmented wart about the face or neck is quite harmless (Fig. 87).



FIG. 88.—Endothelioma.

Endothelioma is a sarcoma arising from the rather specialized connective-tissue cells lining vessels, spaces and serous cavities. These endothelial cells have some of the properties of epithelium, including secretion and cell formations. The endotheliomata, accordingly resemble the carcinomata in some respects. They frequently arise in the endothelium of bloodvessels (*hemangio-endothelioma*) or of lymph vessels

(*lymphangio-endothelioma*). A particular form with whirls around bloodvessels, presumably arising from the endothelium of the perivascular lymph channels has been called *perithelioma*. As a further illustration of the multiplicity of terms, cylindroma is applied to such whirled-cell formations with a peripheral hyaline degeneration, thus forming cylinders. Endothelioma cannot be distinguished clinically from other sarcomata (Figs. 88 and 89).



FIG. 89.—Round-cell sarcoma of shoulder.

A great variety of terms in connection with sarcoma descriptive of some inessential may be found in the literature, but the above-mentioned types are quite sufficient.

EPITHELIAL TUMORS.

Benign Tumors of Epithelial Origin.—**Papillomata.**—Papilloma is applied to the benign tumor of the surface epithelium, skin or mucous membrane. It is primarily an epithelial growth with a secondary proliferation of connective ti

forming a central core as in the ordinary wart (Fig. 90). The surface epithelium is thrown in folds, producing a corrugated surface. Transverse sections of the downward projections of the epithelium obviously would appear as



FIG. 90.—Pedunculated melanotic papilloma. The epidermis contains pigment in the deeper layers. The embryonal cells are free from pigment. (Hertzler.)

islands of cells, which on superficial examination resemble malignancy. However, there is no breaking through the basement membrane nor the other signs of malignancy. The mucous membrane shows growths varying from a slight nodular protuberance arising at a point of irritation, to long finger-like processes consisting of several layers of epithelial cells around a central fibrous core. The epithelial proliferation is primary and may be very active, leading out a supportive strand of connective tissue as it grows. These papillomata have a definite tendency to malignant change. They occur not infrequently in the urinary bladder causing annoying hemorrhage. They also occur very typically on the inner wall of cystic tumors, forming the well-known *papillary cystoma*, which is frequently seen arising from the ovary. Sooner or later these show malignant qualities. The papillary epithelium grows through the cyst wall and may be carried all over the peritoneum, where it may be implanted and form a secondary growth. This is known as implantation metastasis. The main importance of the papillomata lies in their possibilities of malignant change. The same considerations apply here as in melanotic sarcoma, arising from the connective-tissue elements of these skin and connective-tissue growths, especially the pigmented ones. There may also be melanotic carcinoma. Usually the malignant change in papilloma results in the unpigmented skin cancer—epithelioma.

Adenoma.—Adenoma is a benign tumor of glandular epithelium. The growth retains something of the original structures of the gland from which it arises (Fig. 91). This may be acinous or tubular or solid when there are no lumina in the gland as in the liver. The acini are atypical in arrangement, but are definitely limited by basement membranes so long as the tumor is benign. The specific secretion is lost, but since functional activity is not all replaced by reproductive activity in a benign tumor, there remains a certain amount of modified secretion in many instances. This may be retained within the acinus or dilated tubule, producing the so-called *cystadenoma*. Within this papillary processes may develop as just described. This would then

be called *papillary cystadenoma*. If it should become malignant the whole pathological process would be designated by the term *papillary cystadenocarcinoma*. Synonyms, such as *cystadenopapilliferum malignum* in this case, have no added significance. It is inevitable that a multiplicity of terms should arise in the literature of tumors. Adenomata are widely distributed. They are frequent in the mammary gland, where they have a great tendency to cancerous change. Adenomata of the thyroid gland are

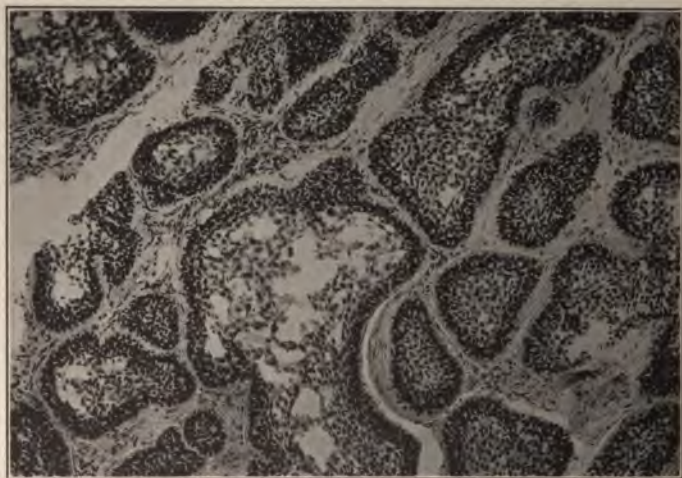


FIG. 91.—Adenoma.

often seen in simple goiter. Adenoma of the salivary glands occurs, but much less frequently than the characteristic mixed tumors previously described. The mucous and sebaceous glands occasionally give rise to adenomatous growths as well as cysts. The mucous membrane of the gastro-intestinal tract, the kidney, the uterus and ovary are other frequent sites of adenoma. *Hypernephroma* is a special form of adenoma of the kidney arising in embryonic rests of cells from the cortex of the adrenal gland. It occurs as an encapsulated tumor, usually at the upper pole

of the kidney, sometimes farther displaced. It may attain great size and readily becomes malignant.

Malignant Tumors of Epithelial Origin.—Malignant epithelial tumors or carcinomata are, strictly speaking, cancer, although the latter term is used loosely to mean any malignant tumor. As stated, they occur in the second half of life. There are exceptions. When cancer occurs in younger people it is very apt to be rapidly growing and highly malignant.

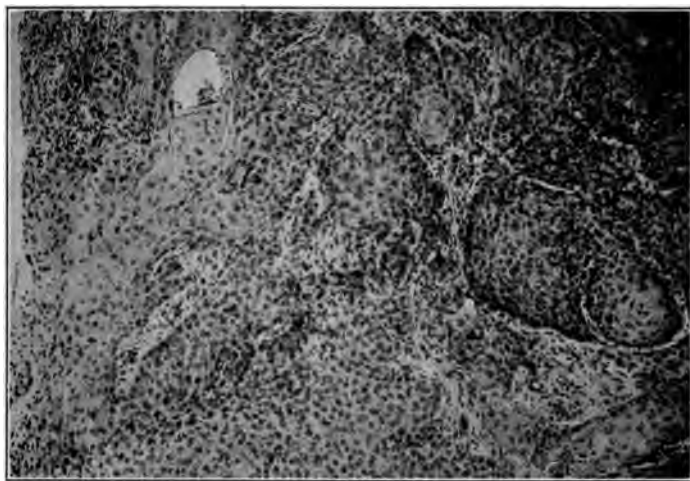


FIG. 92.—Epithelioma, with epithelial pearls.

Epithelioma.—Epithelioma is applied to malignant tumor of the squamous-celled surface epithelium. The term is not distinctive of malignancy as papillocarcinoma would be, but it is an established usage to speak of epithelioma of the lip or tongue, meaning always the malignant growth. The epithelial cells have little or no tendency to metaplastic change. Squamous cells remain squamous in the metastases; columnar remain columnar. Epithelioma develops as downward growths or finger-like projections of the surface epithelium into the subcutaneous tissue, showing early the wild

lawless features of the high-grade malignancy which these skin cancers possess. As the projections grow downward, the surface cells, the flat squames are invaginated and surrounded by a column of more rounded cells from the deeper layers, such as the Malpighian layer. As growth goes on, the central squames are more and more compressed, flattened and keratinized, forming a very characteristic refractile body known as the epithelial pearl (Fig. 92). These pearls show more or less hyaline degeneration and stain deeply with eosin. They are conspicuous objects in sections and aid in the diagnosis of squamous-celled carcinomata or epitheliomata. Epithelial pearls, however, are not necessarily present, especially in the rapidly growing tumors, in which there is not sufficient time for their formation. Cells of the tissues adjacent to an epitheliomatous process early show degenerative changes as evidence of a chemical cytolytic process at work preparing for the actual invasion of the cancer cells, and probably also supplying them with nutrition to some extent. The most active growth is at the periphery but continues also at the center, so that sooner or later necrosis occurs and ulceration. These pathological processes thus explain the clinical picture of epithelioma, as seen typically, for example, in the lips. A small papule appears either as a papilloma at first, or a primary epithelioma, often at a point of irritation. This grows steadily, becomes quite hard with induration of the surrounding tissues and ulcerates fairly early (Fig. 93). Metastasis to the submaxillary lymph glands takes place so early that by the time the diagnosis can be made clinically cells have usually escaped. It has become a recognized surgical treatment to remove these regional lymph glands at the same time the original growth is removed. Otherwise secondary tumors appear later in the glands and then the opportunity for radical removal and cure has gone. Epithelioma similarly may appear on the tongue or inside of the cheek opposite a snag of tooth. There is no type of tumor where the obligation for early recognition is so urgent.

Responsibility of the Dentist—The dentist may see epitheliomata first, and it is important for him to understand that

temporizing may be fatal. Traumatic ulcers which enlarge and become indurated after the cause is removed should always be looked upon with suspicion. Papillomata, which

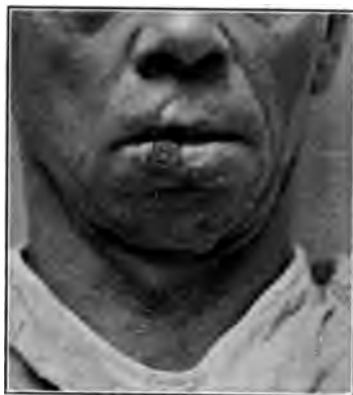


FIG. 93.—Epithelioma of lip, early stage.



FIG. 94.—Epithelioma of lip, later stage.

show activity or are so situated as to be chronically irritated, should be excised and examined microscopically. Patches of leukoplakia, a bluish-white thickening of the mucous membrane, are also beginning points of epithelioma. If activity

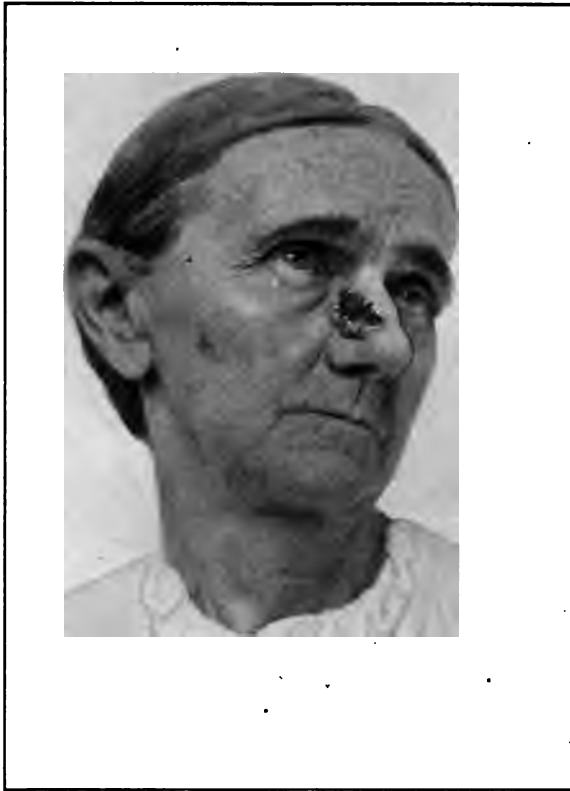


FIG. 95.—Basal-celled Epithelioma of the nose or rodent ulcer; the upper border is healing, while the lower border is extending. (Hertzler.)

is manifested at any one point by greater thickening and induration, it should be excised. The later stages of epithelioma of the mouth are associated with the most foul sloughs and decomposition. Hemorrhage is frequent and cachexia may be extreme (Fig. 94).

Special Types of Epithelioma—Rodent Ulcer or basal-cell carcinoma of the skin is a very different kind of growth from typical epithelioma. It arises from the basal cells of the epidermis or from the hair follicles. The main feature is the extreme chronicity of the process. It may last ten to twenty years without forming metastases and without invad-

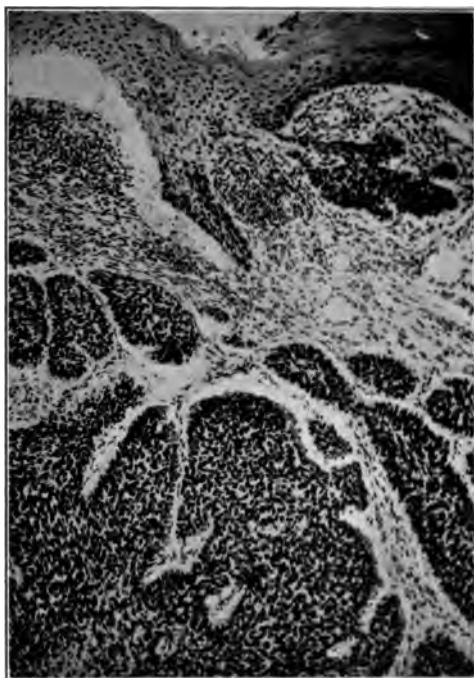


FIG. 96.—Rodent ulcer.

ing surrounding parts extensively. It appears first as a small nodule in the skin, nearly always in the upper part of the face around the nose, eyes and ears, then breaks down to form the characteristic chronic ulceration—a rather deep crater (Fig. 95), with irregular hard, everted edges and a smooth reddish-gray floor. Microscopically the cell columns are

small, irregular and show no epithelial pearls. There is fibrosis and contraction in the surrounding dermis, which may act to some extent mechanically to prevent escape of cells to the deeper lymphatics. There is never the scar formation, however, that occurs in lupus. Rodent ulcer rarely causes death. There is no cachexia and many old men die of natural causes after having had them for years. If they are removed as they should be in people in good general health, it must be done very thoroughly since active growth may follow incomplete removal.

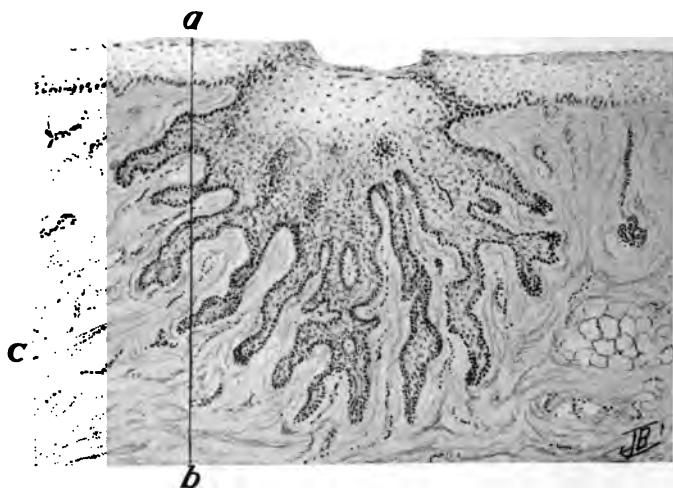


FIG. 97.—Schematic drawing of a carcinoma, showing how a section in line *a-b* would show apparent cell nests, while really the cell columns are connected with the main portion of the tumor. (Hertler.)

X-ray Carcinoma results from repeated exposure to the *x-ray*, following chronic inflammatory processes in the skin and the stimulation of the epithelial cells. The cells are somewhat intermediate in type but in general the histological structure resembles the squamous epithelioma. It has marked infiltrating power and gives rise to extensive metastases. The epitheliomatous process usually follows after prolonged fibrosis, keratosis and often ulceration. Advantage

has been taken of this artificially produced cancer to study the etiology of cancer experimentally, but so far it does not seem to make the subject any clearer. A number of pathological processes precede the actual epithelioma, such as injuries to the cells of epithelium itself and of bloodvessels and true skin with the production of abnormal chemical substances and cytolytic toxins. Attempts at regeneration from these injuries are at work, so that the problem of etiology is still quite a complicated one (Fig. 97).

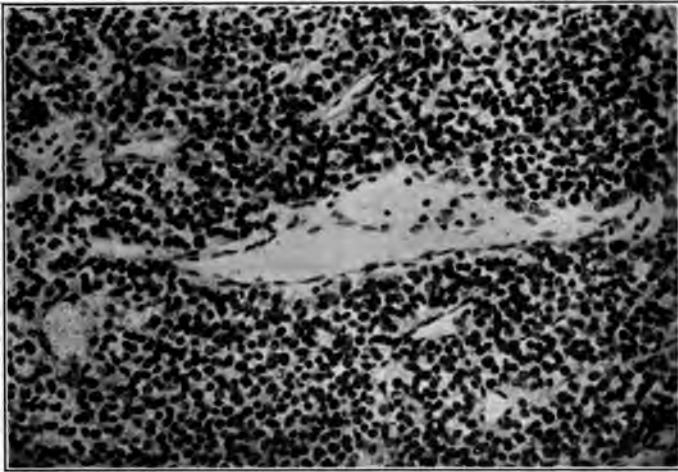


FIG. 98.—Carcinoma of thyroid.

Adenocarcinoma is the malignant growth of glandular epithelium. Some semblance of the type of gland structure is retained, whether tubular, acinous or solid. Instead, however, of a regular acinus, wild irregular outlines are seen with piling up of the lining epithelial cells. When malignant changes develop in adenoma, one of the earliest microscopic evidences is the breaking through the basement membrane by proliferating epithelial cells. Adenocarcinoma is frequent in the breast and in the gastro-intestinal tract and in other mucous lined organs. The degree of malignancy varies considerably but in general, the growth is quite rapid and

metastasis occurs early. It is the commonest form of cancer of the breast, in which early breast amputation and primary removal of axillary glands and fat are necessary for radical cure. In this connection it may be stated that all tumors of the breast should be removed for if they are not already malignant, they may become so and perhaps more regularly in this than in any other organ. Cyst formation often occurs and the previously mentioned papillary cystadenocarcinoma. Within these hemorrhages and liquifactive necrosis

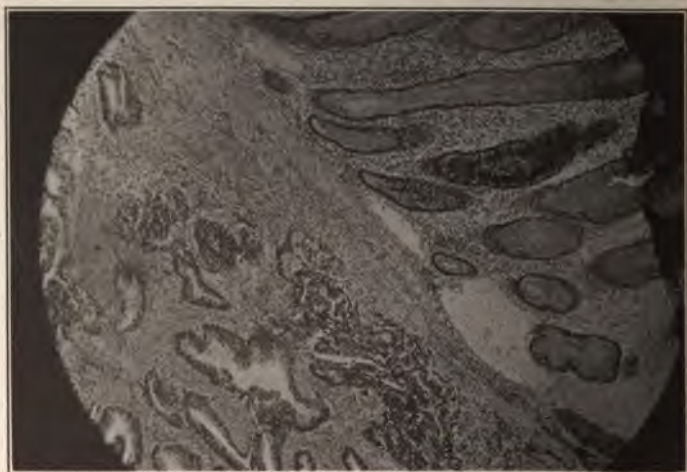


FIG. 99.—Adenocarcinoma.

are frequent. Myxomatous change may occur and a closely related condition known clinically as *colloid cancer* in which there is marked production of gelatinous and mucinous material. With these forms in the abdomen, implantation metastases all over the peritoneal surface are frequent. They sometimes extend through the diaphragm and spread over the serous membranes of the chest. This has been termed *general carcinomatosis* or *carcinosis*.

General Classification of the Carcinomata—Carcinoma in general may be divided into two kinds on the basis of struct-

ure, regardless of the source of the growth. These are *medullary* and *scirrhous* (Fig. 100). The medullary (like medulla or marrow) form is a soft, highly cellular rapidly growing and very malignant tumor comparable to the small round-cell sarcoma. In fact, these two most malignant of all tumors—medullary carcinoma and small round-cell sarcoma—approach each other very closely in structure. All attempts at cellular differentiation are lost and the intercellular substance of sarcoma is not seen. Both show simply a dense

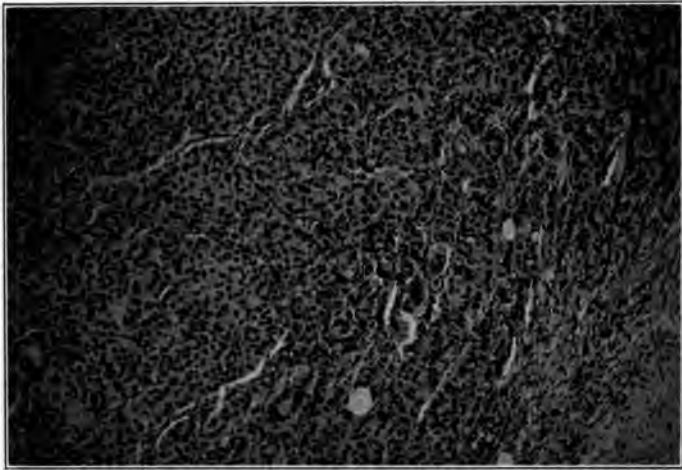


FIG. 100.—Medullary carcinoma.

mass of round, rapidly dividing cells. In these forms too the characteristic mode of metastasis is less constant and rapid generalized dissemination is frequent. Medullary carcinoma is more apt to occur in younger people, in whom rapid growth and high malignancy of tumor are more frequent. They form bulky masses, which soon involve the overlying skin and break down in large fungating ulcers. As stated before, these growths should never be massaged or squeezed on account of the danger of expressing cells into the lymphatics or circulation. Early radical operation is

the only hope of cure. A mass of medullary cancer is sometimes similar in appearance and consistency to brain sub-

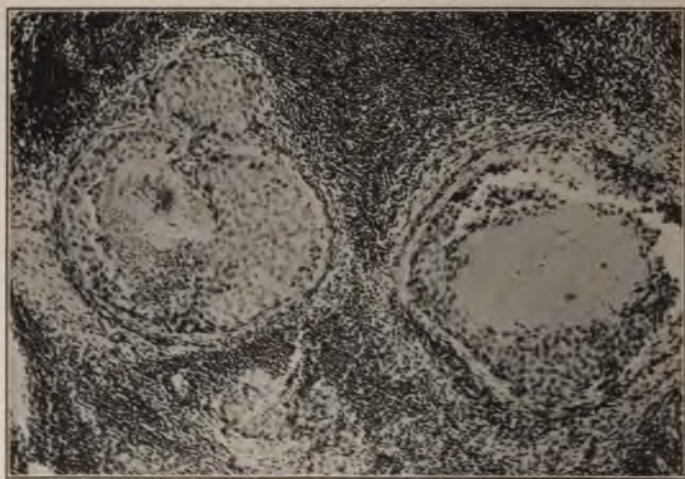


FIG. 101.—Secondary carcinoma.



FIG. 102.—Scirrhous carcinoma.

stance and even show the surface convolutions giving rise to the term *encephaloid* (*brain like*) cancer. As in sarcoma a great variety of terms have arisen in the nomenclature of cancer and have no greater significance. The other form of cancer, the scirrhus (hard) represents the opposite extreme. It is an extraordinarily slow growth with marked fibrous tissue formation, which later contracts and produces general shrinkage of the affected organ and distortion of its parts. The overlying skin and the nipple in the case of scirrhus of the breast are retracted. This form of cancer occurs in older individuals as a rule and may last ten years or more. Microscopically, cancer cells are relatively few and embedded in dense bundles of fibrous tissue. These bundles may be seen to run in all directions forming compartments, in which nests of cells are confined. Metastasis takes place slowly although ultimately in some cases is extensive. It may occur by extension along the subcutaneous lymphatics forming multiple nodules or at times causing a diffuse hardening and stiffening of the skin. The latter form has been called *cancer-en-cuirasse*. This usually occurs from scirrhus of the breast. The skin involvement may extend up over the neck. *Carcinoma simplex* is a term applied to a form midway between these two extremes, neither the cellular or fibrous elements predominating. There are of course intermediate forms in great variety.

CYSTS.

There remain to be considered only a few irregular growths, some of them not true neoplasms. They may be grouped under the heading of cysts or sack-like structures containing liquid or secretion of some kind.

Retention Cysts result from simple obstruction to the outlet of a gland. The best example is the wen or sebaceous cyst, which is the commonest tumor of the scalp (Fig. 103). They vary in size from that of a small pea to an egg and may be multiple. They occur also on the face, neck and back and in fact any part of the skin where there are sebaceous glands. They resemble small lipomata, except that they are adherent to the skin and are not lobulated like a lipoma. The putty-

like consistency of the contents can usually be felt. They may become infected and inflame and discharge like an ordinary abscess, sometimes leaving a sinus. The sack may be excised or destroyed by caustics. Occasionally a true neoplastic process arises in the cells of the sebaceous gland. Malignancy may result from chronic irritation in infected sebaceous cysts.



FIG. 103.—Wens or sebaceous cysts.

Comedones, or "black heads," about the nose and face are minute retention cysts of the sebaceous glands.

Miliaria, also called *sudamina*, is a similar condition of the sweat-glands producing pinhead-sized transparent cysts in the skin. Small retention cysts of the mucous glands of the lips and mouth are frequent and require only a simple puncture.

Ranula is a term applied to cysts in the floor of the mouth usually of the mucous glands. There may also be retention cysts of the salivary glands, as from stone in the ducts. They may occur in the breast, kidney, pancreas or any glandular organ.

Congenital Cysts arising from tubular and other embryonic structures present quite a variety of forms. They may develop in later life. In the neck there are the thyrolingual cysts from the primitive thyrolingual duct extending from the thyroid gland to the foramen cæcum of the tongue. Cysts with more or less thyroid tissue may occur at any point along this path, but most commonly present in the midline near the hyoid bone. Branchial cysts from the primitive branchial clefts occur in the region of the sternocleidomastoid muscle from the ear down. Mucous or sebaceous material results from the inclusion of epithelial cells. The latter occasionally undergo malignant changes, giving rise to the so-called branchiogenic carcinoma—a primary cancer in the neck. In the urachus, the omphalomesenteric duct and many tubular structures remaining from the early development of the genito-urinary system, cysts may occur. Hydrocele is an accumulation of serous fluid in the normal tunica vaginalis. It may be congenital, or develop later in life sometimes following injury.

Liquefaction Cysts result from necrosis and solution in the center of solid tumors or inflammatory processes. Hemorrhage into certain tissues may become encapsulated and the blood products remain as cystic contents. Lesions in the brain are particularly liable to undergo liquefaction and cyst formation. A hemorrhagic cyst of the brain may gradually change to a clear serous cyst by absorption of the blood elements.

Parasitic Cysts result from the tissue reaction to the irritation of parasites. *Trichini*, the cause of pork poisoning, are minute worms which become encysted in large numbers in the muscles all over the body (Fig. 104). The diaphragm may be so involved as to cause dyspnea. The skeletal muscles are tender to the touch. The masseter and other muscles of mastication may be so tender and spastic as to give rise to a considerable degree of trismus and from interference with the lymph flow to edema especially about the eyes. *Echinococcus cysts* result from a parasitic worm originally from the dog. It is rare in this country but more frequent in the Orient. Large cysts with many compart-

ments (multilocular cyst), containing a gelatinous substance and elements of the parasite, are found usually in the liver, but may be widespread even in the brain.



FIG. 104.—*Trichinella spiralis* in muscle, greatly magnified. (Simon.)

Dermoid Cysts have been mentioned as examples of growths from embryonic rests. They occur along lines of fusion where cell inclusions would be most probable. They are characterized by the presence of modified epithelial structures in their contents, such as hair, nails and elements of teeth. They occur in the midline of the body and along the

lines of fusion of the facial clefts. *The sacrococcygeal dermoid* is a frequent form occurring just over the coccyx. It may become inflamed repeatedly and discharge, leaving a fistulous opening which requires complete excision for cure. Dermoid may occur in the hard or soft palate in or near the median line or in the pharynx. They are covered with skin and are often hairy. The ovary is the seat of large dermoid cysts and of the still more complex formations from fetal inclusions known as teratomata (monster tumors). The latter represent all of the primary germinal layers. Besides epithelial structures, as in dermoids, there may be fingers, coils of intestine, part of a jaw with teeth and even a large part of another fetus.

Neoplastic Cysts, Cystoma.—*Adenocystoma* are forms in which there is true tumor formation associated with cystic contents. It is more than simple retention by mechanical obstruction of the duct of a gland. These cysts occur in ductless glands such as the thyroid. The most frequent site is the ovary.

Ovarian Cysts are frequent, and if not operated may attain enormous size, even exceeding the rest of the body in weight. They contain a mucinous substance, usually clear. They may become twisted on their pedicle and strangulated, causing acute abdominal pain and signs of peritonitis. These cysts may be unilocular or multilocular. Papillary growths from the walls of simple cystoma produces papillary cystoma, which has already been described. It may be repeated that there is a great tendency to malignant change (papillary cystadenocarcinoma) in this growth even in young girls.

TERATOMATA.

Teratomata may occur in a great variety of forms in addition to the above-mentioned teratomatous cysts. They really represent a second fetus growing as a parasite upon the body. They are due to a very early division of the primary germinal cells into two parts, as occurs in single ovum twin pregnancy. This division must occur while the primitive cells are still totipotent, that is

germ layers of the embryo. In teratoma one embryo early overgrows the other, which then is included as a parasite and usually at locations of embryological fusions as stated under dermoids. All manner of monsters occur in this way—attached fingers, toes, teeth, arms and conglomerations of organs. Sometimes they are attached to the roof of the mouth by a pedicle and protrude from the mouth. This is known as *epignathus* (upon the jaw). The sacrococcygeal region is also a frequent site. A lone finger projecting at this point in a newborn infant is not very rare. It may be readily removed. Teratology deals with these monstrosities and their embryological development.

CHAPTER XV.

SPECIAL PATHOLOGY OF THE ORAL CAVITY.

CONGENITAL ANOMALIES.

Special pathology refers to manifestations of general pathological processes in particular organs or locations. Under the above heading may be brought together the



FIG. 105.—Cleft palate.

various lesions and conditions of practical importance seen in the mouth. Many of them have already been described in detail and will only need to be mentioned. *Malformations* are considered fully under oral surgery. Here it may simply be noted that they are due, as most congenital malformations are due, to incomplete embryological processes. In hare-lip and cleft palate (Fig. 105) there is an imperfect fusion of

the fronto-nasal and superior maxillary processes. For this reason hare-lip is always to one side of the median line and the intermaxillary bone carrying the upper central incisor teeth may project forward from the end of the frontonasal process. Rarely there is a median cleft in the lower lip and jaw, because these fuse normally in the midline. Occasionally there is a *small undeveloped mandible* on one or both sides. When unilateral it produces marked facial asymmetry. The flare of the angle of the jaw away from the midline may be so much less than on the normal side that the



FIG. 106.—Congenitally undeveloped right mandible. The distance of the angle of the right jaw to the symphysis mentis is much less than on the left side. The flare of the jaw from the midline is also much less on the right side, leaving redundant skin in the region of the ear and partially closing the external auditory meatus.

overlying soft parts are relaxed and atrophic (Fig. 106). *Epignathus* (upon the jaw) is described under teratomatous tumors. It consists of a growth from the midline of the palate and may protrude from the mouth. It may be part of another fetus.

ACQUIRED ANOMALIES.

Acromegaly described under hyperpituitarism is an acquired hypertrophy of the bones and overlying soft parts of the face

especially the lower jaw. There is spacing of the teeth. The coarse quality of the voice and overgrowth of hands and feet make a very characteristic picture. *Torus palatinus* is a median ridge in the hard palate representing an overgrowth of bone along the line of fusion. It has no significance. Obstruction to nasal breathing causes a high, narrow palatal arch.

Lesions of the Lips.—The *lips* show a variety of lesions with which the dentist comes in direct contact. Simple *fissure*



FIG. 107.—Herpes labialis.

or cracking of the lips is a painful condition and provides an atrium for infections. *Herpes labialis* (Fig. 107) frequently called "cold sores," consists in a crop of vesicles, later changing to crusts and scabs due to disturbed trophic nerve influence. Distinct tenderness of the part precedes the actual eruption. It is most commonly associated with respiratory infections, especially pneumonia. Small herpetic lesions including the so-called "chancre sores" are frequently due to minor digestive derangements and constipation. They

may be exquisitely tender, especially when located at a very movable point on the lips or tongue. They occur anywhere in the oral cavity. *Eczema* of the face and lips sometimes leads to marked thickening and stiffness about the mouth, so that dental work is impossible until the condition is controlled. *Eczema* is characterized by itching, serous exudation from the lesions and inflammatory thickening of the skin. It is not infectious, except for the secondary skin cocci in the crusts. *Mucous cysts* appear on the lips as clear pea-sized tumors, due to retention of mucus in one of the many mucous glands in the substance of the lip.

Chancre, or primary syphilis of the lip, is probably the most frequent extragenital chancre. It usually occurs in a fissure or some smaller defect in the mucous membrane, most frequently contracted by kissing, but also from contaminated dishes, towels, pipe-stems, pencils and other objects and instruments coming in contact with the lips. The lesion has the same hard gristle-like feel described in the chapter on syphilis, and on the mucous surface a grayish pellicle, perhaps a half inch in diameter, which helps in the diagnosis. The sore is of a few weeks' duration and there is early involvement of lymph glands, which may in a month's time reach the size of walnuts. The surface is teeming with spirochetes, which may readily be seen in the exuding serum by means of the dark field illuminator. Of course no dental work could be done until constitutional treatment was carried out. The latter if thorough prevents the appearance of the secondary mucous patches in the mouth. Chancres have occurred rarely in the tonsillar region and other parts of the mouth. Late syphilitic lesions may occur on the lips as crescentic or annular eruptions or single larger ulcerations.

Epithelioma, or cancer of the lip, should always be thought of at once in a patient past middle life presenting a small warty growth on the lower lip. It may be the size of a small pea and of two months' duration before the patient pays much attention to it. Ulceration occurs early. There is practically no pain or inflammatory reaction in the early stages. When the submaxillary lymph glands are enlarged the growth is rapidly approaching an inoperable state. Within

the oral cavity, epithelioma occurs on the tongue or on the inside of the cheek, especially in a leukoplakial patch or simple ulcer. Ulceration is very early in the mouth, and these so-called epitheliomatous ulcers have the characteristics of malignancy mentioned before—sharp, indurated edges and tendency to bleeding with slight injury.

Tuberculosis is a rare lesion on the lips, but does occur in cases of chronic pulmonary tuberculosis. Tubercle bacilli in the sputum lodge in a fissure and produce a chronic ulcer of the pale, indolent type previously described. Tuberculous ulcers, however, are seen more often on the tongue and palate, although, as stated before, oral tuberculosis is rare considering the great frequency of pulmonary disease. Most cases are seen in association with advanced pulmonary and laryngeal tuberculosis.

Lupus, the chronic fibroid tuberculosis of the skin producing scars similar to those of a burn, may occur on the lips. Finally cyanosis and anemia may be recognized in the mucous membrane.

Lesions of the Gums.—The *gums* are very sensitive structures and react to many systemic intoxications. The *metallic poisonings* of lead, mercury, bismuth and arsenic have been sufficiently emphasized. The spongy, swollen, bleeding gums of *scurvy* are the main diagnostic feature of that disease. Forms of pyorrhea secondary to constitutional disease are very frequent and somewhat characteristic of the disease in some conditions. Diabetes, for example, is sometimes associated with a marked suppurative gingivitis and falling out of the teeth. True *pyorrhea alveolaris* is poorly understood in regard to its etiology. Hopewell-Smith believes it is primarily an atrophy of the alveolar process with a secondary gingivitis. Constitutional and local infective factors undoubtedly come into play. The subject is in much the same uncertainty as pernicious anemia, which is called primary anemia because its etiology is not definitely known. A simple *stomatitis*, or inflammation of the mucous membrane of the mouth, such as frequently occurs in children with digestive disturbances and infectious diseases, is most intense along the margin of the gum. Swelling

ing and ulceration may become severe and interfere with the general health.

Lesions of the Tongue.—The *tongue* is also a mirror of the general bodily condition and especially of the gastro-intestinal tract. *Coating* of the tongue, besides digestive derangements, occurs in almost any acute or chronic intoxication or infection. The color and character of the coating have diagnostic value. The "septic" tongue is dry and brown; in rheumatic fever there is a moist white coating. Chronic ulcer of the tongue, as noted before, is nearly always one of three conditions, gumma, cancer or tuberculosis. The differential points have been indicated. Microscopic examination is sometimes necessary to make the diagnosis. The therapeutic test with potassium iodide and mercury curing the gumma at once establishes its nature.

There is also a chronic *interstitial glossitis* due to tertiary syphilis leading to sclerosis of the tongue from fibrous tissue overgrowth and puckering of the surface from cicatricial contraction. *Leukoplakia* is a very common condition, consisting in irregular white patches on the mucous membrane of the tongue, cheek and lips. It has the appearance as if the tissues were partly coagulated by heat. Its nature is not very clear but is related to chronic irritation, as by tobacco and alcohol and jagged teeth. Syphilis is regarded by some as a factor, but certainly is not present in all cases. It is more closely related to the cancerous process, and epithelioma often begins in a thickened leukoplakial patch.

Geographical tongue is a striking condition of circinate, map-like marking of the mucous membrane due to partial desquamation and subsequent healing in the center. There is no disturbance of general health and at most local itching. It may continue for years. It is important to know that there is a form of syphilitic glossitis that resembles geographical tongue very closely. Another rare and perplexing condition is *black or hairy tongue*. There is a marked hypertrophy of the filiform papillæ giving the hair-like appearance. The black color is due either to a deposit of pigment or to the growth of a dark colored fungus such as *Aspergillus niger*.

Tumors.—Benign tumors of the tongue occur, including *hemangioma* (usually a blue mass or network of veins) and *lymphangiomas*. The latter may be a very diffuse process, producing marked enlargement of the tongue (lymphangiomatous macroglossia), which is subject to recurrent attacks



FIG. 108.—Ranula forming a lobulated mass under the tongue. (Hertzler.)

of inflammation. *Lingual goiter* is a rare growth from aberrant rests of thyroid tissue in the region of the foramen cecum, which represents the end of the primitive thyroglossal duct. *Ranula* is a cystic tumor under the tip of the tongue on the floor of the mouth, arising from the mucous or

salivary glands (Fig. 108). Stone in Wharton's duct causes swelling in the floor of the mouth and in the submaxillary gland, and pain during eating because of obstruction to the increased flow of saliva. *Tongue-tie* in infants due to a short frenum linguæ rarely requires any interference. The frenum lengthens as the child grows. *Atrophy* of the tongue results from lesions of the hypoglossal nerve or its nuclei of origin in the medulla or bulb as in bulbar palsy. In this condition the tongue lies flaccid in the floor of the mouth and there is drooling of saliva. The process is usually unilateral, at first causing hemiatrophy linguæ and protrusion of the tongue to one side.

Oral Lesions in the Eruptive Diseases (Exanthemata).—
Measles.—The oral cavity shows lesions in a number of the specific infectious diseases, especially the acute exanthemata. *Measles* is essentially an acute catarrhal inflammation of the conjunctiva, nasopharynx and upper air tract. This process goes on with the symptoms of a feverish cold for four days or more before the skin eruption of measles appears. During this stage and several days before the skin eruption there appear in the mouth characteristic lesions known as *Koplik spots*, which are diagnostic of measles. They are small, milky white spots or minute vesicles, surrounded by a red areola, and occur most frequently on the inside of the cheek opposite the molar teeth. Once seen the dentist may readily recognize Koplik spots and avoid the contagion of measles. The marked conjunctivitis or red eyes of the early stage of measles are very characteristic, although a simple nose cold may extend up the nasal duct and cause conjunctivitis. A child with Koplik spots should, of course, be put to bed and isolated. Mild cases that are up and about during this stage may develop a fatal pneumonia. They are also responsible for the spread of the infection, which is very easily transmitted in the mucous secretions. The infectivity is also greatest in the pre-eruptive stage when the Koplik spots are most prominent. Monkeys may readily be inoculated with measles by spraying the nostrils with the nasal secretions from a patient. *German measles* is a separate disease and does not show the Koplik spots, although there

is redness of the throat and a catarrhal inflammation of the nasopharynx of moderate degree. There is marked enlargement of the lymph glands, especially of the postcervical group. The disease differs also from ordinary measles in the appearance of the skin rash on the first day of the disease. It is a mild infection.

Chicken-pox (Varicella) and *Small-pox* (Variola) also have lesions in the mouth and other mucous membranes as well as on the skin, much less abundant, however. They occur as vesicles an eighth to a quarter inch in diameter, which break open, forming ulcers with a zone of redness around



FIG. 109.—Variola. Stage of eruption. (Courtesy, Dr. S. Dana Hubbard.)

them. They are often seen in the palate. The skin lesions are more distinctive (Fig. 109). Chicken-pox is mild and is important mainly because it is often confused with mild smallpox. Chicken-pox is not preceded by any constitutional symptoms, while in small-pox, fever, chill and grippelike symptoms occur in the week previous to the eruption. When the disease is not prevalent the diagnosis can hardly be made at the outset. The great majority of the cases are seen in those who have never been vaccinated. The lesions are most abundant on the face and hands and feet, including the palms and soles, unlike chicken-pox. The lesions of small-pox are hard and shotty; those of chicken-pox are

superficial vesicles drying up in the form of blackish scabs. The contagion is of high grade in both diseases.

Scarlet fever is essentially a throat infection or a systemic infection associated with a throat inflammation. A virulent streptococcus is the main organism found in the throat and no more specific organism has as yet been found. In groups of streptococcus tonsillitis cases or of influenza an occasional scarlatiniform eruption occurs as also following operations in the mouth or throat (surgical scarlet fever), showing that the relation is very close. A very severe angina may occur with marked enlargement and suppuration in the submaxillary lymph glands. It is also very characteristic of the scarlatinal throat inflammation to extend through the Eustachian tube and cause middle-ear abscess. Chronically discharging ears often result and the pus may transmit the disease for a long time. The eruption is a diffuse scarlet flush over the whole body in typical cases. It follows a day or so after a rapidly rising temperature and sore-throat. There are many mild cases, which may give rise to the most severe forms of the disease in others. It is therefore one of the many things the dentist must consider in dealing with the patient with sore-throat.

Oral Lesions in the Non-eruptive Diseases.—Among the non-eruptive diseases, *whooping-cough* and *influenza* have a pathology similar to that of measles, namely, a diffuse catarrhal inflammation of the throat and upper air passages. The secretions are highly infectious. During an epidemic of influenza the organisms are found in the mouths of a large proportion of people generally ready to set up an inflammatory process at any time when the general resistance is lowered, as by exposure to cold. Obviously the dentist is much exposed when constantly working in the mouth.

Diphtheria is a throat infection with the specific bacillus of Klebs-Loeffler, forming a purulent membrane at various points, usually first in the tonsillar region then extending to the nose or larynx. The extension beyond the limits of the tonsil upon the soft palate and uvula is at once suggestive of diphtheria. It may be primary in the nose or larynx. The membrane is of a dirty gray color, is adherent to the under-

lying tissues and gives off a most offensive, almost fecal odor. The toxemia of the disease is profound and death is produced by paralysis of the heart muscle. Before the use of antitoxin, diphtheria was one of the most fatal of the throat infections, and still causes many deaths every year, mainly due to late diagnosis and late antitoxin treatment. All throat infections with spots or membranes should be cultured and the condition regarded as having serious possibilities. Early antitoxin treatment of diphtheria usually results in prompt recovery, but the eradication of the infection is at times very difficult. The diphtheria bacilli may persist many months in the throat, especially in the crypts of the tonsil in spite of antiseptic gargles and local applications. These cases are the so-called "*carriers*" which are being found more and more to perpetuate a number of the infectious diseases. Tonsillectomy is sometimes justifiable to overcome the endless "positive" cultures after diphtheria.

Cerebrospinal meningitis gains entry through the nasopharynx probably through the cribriform plate of the ethmoid, and many meningococcus carriers have been found in military camps not only in convalescents from the disease but also in "contacts" or persons living near patients. The meningococcus can be cultured from the nose in these cases, so that this highly fatal disease also concerns the dentist. It is seen that he must always have an "aseptic routine" for hands and instruments, since any patient may be a carrier or may be in the incubation stage of some infectious disease.

It is probable that the infective agent of *infantile paralysis*, or poliomyelitis, enters through the throat and respiratory tract and is transmitted from one individual to another just as other infections. During an epidemic there are probably many mild cases without paralysis, which serve to spread the disease. This especially concerns the dentist.

Other Local Infections in the Oral Cavity.—*Vincent's angina*, known also as "trench mouth" because of its prevalence under war conditions, is due to the *Bacillus fusiformis* and the spirillum of Vincent. The evidence now indicates that the two forms are different stages in the development of same organism. It produces a membrane mo-

in the tonsillar region not unlike that of diphtheria, but the constitutional symptoms are very mild. In fact the patient usually notices little more than the local soreness in the throat. The membrane sloughs off, forming a deep ulcer. At times it takes the form of a fissure, extending to the depths of the tonsil. After removing the surface layers of necrotic material, direct smears from deeper parts show the organisms in large numbers. The bacillus is slightly curved and tapered at the ends. Diplobacillus formation is characteristic (Fig. 110). The fusiform bacillus may be grown in

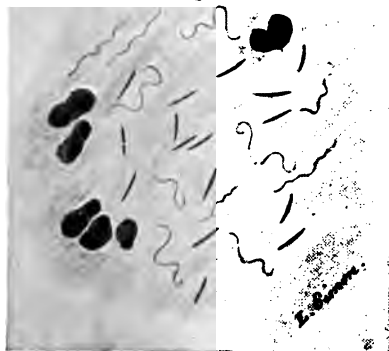


FIG. 110.—Spirochetes and fusiform bacilli in Vincent's angina. (Simon.)

culture under anaërobic conditions. A dilute carbolfuchsin stain is very satisfactory. Smears from carious teeth often show the fusiform bacillus and spirillum together with other bacteria and amebæ. Obviously the organisms of Vincent's angina abound in the mouth. They have frequently been found in the necrotic material of a variety of other lesions, especially in gangrenous stomatitis or noma, a rare complication occurring in severe forms of systemic infections, such as measles, in a very debilitated patient. Ulcerative stomatitis may show the organisms. Vincent's angina is frequently seen in the throats of dentists and dental students. The

assumption is that the infection is carried on the fingers from carious teeth. Fortunately the systemic effect of the disease is usually slight. The slough is foul-smelling and may be extensive, but only occasionally results in permanent deformity of the parts. Lymph-gland involvement is also less than in most throat infections of similar extent. Potassium chlorate seems to have a somewhat specific effect on the process and is used in treatment both locally and internally. Caustics are also used locally.

Thrush is a mouth infection with the fungus *Oidium albicans*. It occurs usually in children in a weakened general condition living in uncleanly surroundings. In institutions, however, such as maternity hospitals, it may occur in epidemic form, affecting healthy infants as well as weaklings. The infection may be carried on milk bottles or nipples and clothing or on the hands. It appears as a thick, white, opaque pseudomembrane, moderately adherent to the mucous membrane of the tongue or cheeks and at times extending to the esophagus or bronchi. It is quite persistent but may be overcome by repeated application of antiseptics. The organism belongs to the order of yeast fungi and consists of branching filaments ending in ovoid cells.

Sprue is a very prevalent tropical disease, probably caused by a fungus closely related to the thrush organism. There are ulcerations on the tongue and in the mouth from which the fungus may readily be obtained. In the south also *pellagra* is characterized by a sprue-like stomatitis, but is not contagious.

Throat Infections.—In the throat proper, simple infection such as by streptococci or pneumococci is very frequent. In the tonsils, *follicular tonsillitis* results from the accumulation of purulent material in the crypts. The infection may extend beyond the bottom of the tonsil and cause suppuration—peritonsillar abscess or *quinsy*. The pus tends to point at the upper pole of the tonsil. It produces tremendous swelling, edema and pain, so that the patient speaks or swallows with the greatest difficulty if at all. It should be remembered, too, that an apparently simple tonsillitis may

be the atrium of infection of many serious diseases, such as inflammatory rheumatism, endocarditis, nephritis, scarlet fever and other conditions.

Chronic tonsillitis as a focal infection is more closely related to certain systemic conditions than abscessed teeth. The tonsils and the related lymphoid tissue on the posterior pharyngeal wall, called adenoids, are enlarged by chronic infection. In children especially, adenoids cause serious obstruction to breathing and impair the development of the jaws and nose as well as the chest. Acute infection in the nasopharynx may lead to a *retropharyngeal abscess*, which bulges forward, lifting the posterior pharyngeal wall some-

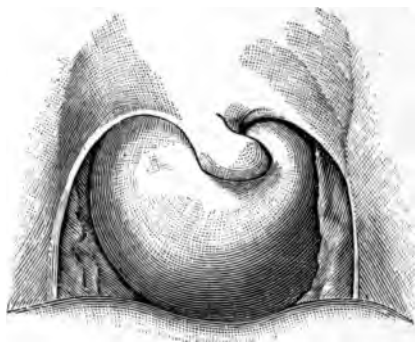


FIG. 111.—Retropharyngeal abscess.

times enough to obstruct breathing (Fig. 111). Tuberculosis of the cervical vertebræ at this level may produce a cold abscess in the retropharyngeal space.

Paralysis of the pharyngeal muscles, and particularly of the palate, occurs at times after diphtheria (*postdiphtheritic paralysis*), so that the patient on swallowing forces liquids back through the nose. The *infectious granulomata* have been sufficiently discussed, but it may be repeated that they may all occur in the mouth and be transmitted through the mouth. *Tumors* have also been considered under the headings of epithelioma, sarcoma of the jaws, epulis, angioma, odontoma and others (Fig. 112).

Lesions of the Salivary Glands.—The salivary glands, especially the parotid, are not infrequently the site of acute infections. *Mumps*, or epidemic parotitis, is highly contagious and transmitted by the mouth secretions. There is no pharyngitis, however, in mumps as in measles and the other infections mentioned. The submaxillary salivary gland is occasionally involved. Suppuration practically never occurs. A non-specific parotitis frequently complicates many bacteremic diseases, such as typhoid fever, pneumonia and sepsis. It may suppurate and require incision and



FIG. 112.—Sarcoma of the jaw, involving salivary glands.

drainage or it may rupture externally or into the ear canal. A chronic parotitis, with enlargement occasionally, is seen in secondary syphilis, in mercurial-poisoning and in other intoxications. Stones or sialoliths occur in the ducts causing the symptoms previously mentioned and when secondarily infected abscesses may form. In the parotid an external salivary fistula is an occasional result. The characteristic mixed tumors of the parotid are the most frequent growths. *Mikulicz's disease* is a rare condition of chronic enlargement of the salivary, lachrymal and buccal glands. It is a hypertrophic or adenomatous process of

CHAPTER XVI.

SPECIAL PATHOLOGY OF STRUCTURES CLOSELY RELATED TO THE ORAL CAVITY.

Lesions of the Cervical Lymph Glands.—The cervical lymph glands are so closely related to the oral cavity that the lesions of the neck structures should be associated with those of the mouth. The lymphatic drainage is very free from the mouth to the regional lymph glands, so that the latter are involved in all acute and chronic infections and in malignant disease of the oral cavity. Acute infections about the teeth and tonsils promptly cause an *acute lymphadenitis* characterized by swelling and tenderness in the affected glands. If the infection is chronic there will be little or no tenderness, but over a period of time there may be considerable enlargement due to an inflammatory hyperplasia of the tissues. This is seen in the *chronic lymphadenitis* associated with persistent infection in tonsils and adenoids as well as in tooth and jaw infections.

Tuberculosis of Lymph Glands.—When the enlargement of lymph glands seems out of proportion to the severity of the primary lesion, or when the glands continue to enlarge after the eradication of the infective focus, it at once becomes suspicious that the tubercle bacillus has found its way to the gland. The local resistance of the glandular tissue is reduced and the tubercle bacillus, carried either directly through the lymphatics from the mouth or in the blood stream from some distant focus of the tuberculosis, is able to lodge and grow in the glands. Tuberculosis of lymph glands is the commonest cause of enlargement or swelling in the neck. It usually attacks the submaxillary group of glands, but may involve the postcervical or supraclavicular glands. The diagnosis is aided by the general symptoms of tuberculosis and by the

demonstration of tuberculosis elsewhere in the body. The course of the disease varies widely as described under tuberculosis. On the one hand, the first tubercles may be obliterated and replaced by fibrous tissue and eventually calcified; on the other hand, there may be progressive enlargement, caseation, secondary infection, abscess formation, multiple fistulæ and generalized tuberculosis. In tuberculous adenitis multiple masses can be palpated, but they are more or less matted together due to inflammation extending to and beyond the capsule (periadenitis). Sooner or later fluctuation due to caseation in the center of the glands is added as a diagnostic sign.

Dental Considerations.—In many practical problems the dentist will have to deal with tuberculosis of the cervical lymph glands. In the first place when the glandular enlargement is not marked there is always some doubt as to whether the condition is one of simple hyperplasia due to mouth infections or whether it is a beginning tuberculous process. Even in tuberculosis of the glands cure would be favored by removal of infectious tooth and mouth conditions, since the local resistance of the tissues would be improved and applied wholly against the tuberculous infection. If secondary infection gains a hold within the glands an acute abscess of the neck results. This either ruptures spontaneously or demands surgical drainage. The usual outcome after this complication is persistent fistulæ leading to the caseous glands. Radical excision may then be necessary for cure. The dentist should know that there are usually other foci of tuberculosis in the body when the glands of the neck are involved, especially when the resistance of the patient is apparently not adequate to overcome the disease. Obviously dental work under such conditions should be limited to the removal of mouth infection.

Hodgkin's Disease.—A disease of the lymph glands usually beginning in the neck and characterized by progressive involvement of other groups of lymph glands—an increasing anemia and a fatal termination. It is probably an infection, although no one organism is agreed upon as the cause of the disease. As diphtheroid¹

and other organisms have been described. The initial enlargement of the cervical glands sometimes follows infections in the oral cavity, especially tonsillitis. The disease runs a chronic course, usually of two or three years. The glandular masses differ from those of tuberculosis in that the

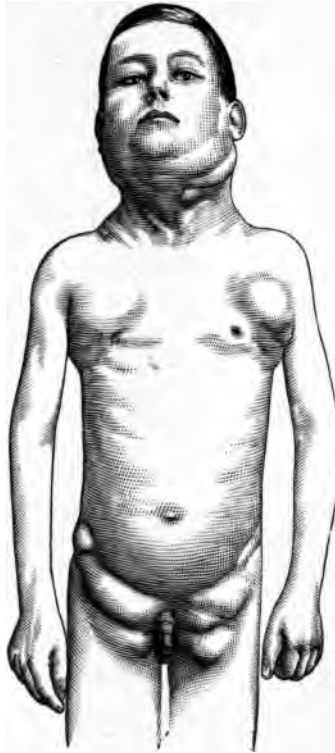


FIG. 113.—Hodgkin's disease. (After Brewer.)

glands are discrete, never matted together. Long chains of individual glands may be followed from one group to another. Caseation does not occur. Microscopically a very characteristic picture is seen in the glands. There are four distinct changes:

- (a) Proliferation of endothelial cells.
- (b) Presence of many eosinophilic cells.
- (c) Formation of giant cells.
- (d) Thickening of the fibrous reticulum.

Any group of lymph glands may be involved, including the intrathoracic groups, which may cause serious symptoms by pressure of vital organs. Usually, however, marked emaciation and cachexia precede death. There may be marked remissions in the course of the disease, especially under arsenic treatment. The only attempt at curative treatment that can be made is the radical extirpation of all

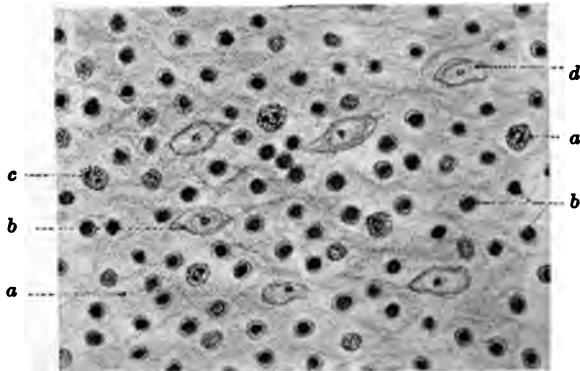


FIG. 114.—Hodgkin's disease: a, endothelial cells; b, eosinophiles; c, lymphocytes; d, connective tissue. (Hertaler.)

the affected glands, together with the focus which might be suspected as the origin or atrium of the infection, such as tonsils or carious teeth.

Leukemia.—It will be remembered that leukemia was described under primary diseases of the blood, the characteristic feature being an enormous increase in the number of white blood corpuscles. There are two forms: the splenomyelogenous form, with large spleen and myelocytes in the blood, and the lymphatic form, with large lymph glands and lymphocytes predominantly in the blood. Leukemia may be related pathologically to Hodgkin's disease. In fact, the

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after has been known as pseudoleukemia. Cases have also been observed to follow spinal infections. The hematological form that comes in connection with the pathology of the lymph glands. In the leukemic cases could not be distinguished from Hodgkin's disease. The microscopic examination of the blood of the tumor gives the diagnosis at once. Leukemia may ultimately prove to be a manifestation of chronic edema with the teeth as one possible portal of entry.



FIG. 115. Lymphosarcoma in a woman, aged twenty-five years. Note the regular margins of the ulcer and fungous granulations of the base. (from Bergmann.)

Lymphosarcoma. This form of sarcoma is not infrequent in the cervical glands. At first it appears as a smooth movable tumor. Gradually it takes on the characteristics of malignancy, invades through its capsule into surrounding structures and becomes a fixed mass. Evidences of increased vascularity with dilated veins on the surface and finally necrosis and ulceration complete the picture of the malignant growth.



FIG. 116.—Tumor of pre-auricular lymph gland.



FIG. 117.—Thyroglossal cyst.

Secondary Carcinoma in Cervical Lymph Glands.—This, of course, is a secondary or metastatic growth originating in the epithelial structures of the oral cavity. The most common source is epithelioma of the lip, tongue or cheek, not infrequently opposite the rough, irritating edge of a tooth. At times the primary growth may be quite concealed until glandular enlargement brings attention to it. This may occur in growths in the antrum or in "fissure cancer" at the root of the tongue. Microscopically, "nests" of epithelial cells may be recognized. The gross features are those of malignancy locally together with marked general cachexia.

Syphilis of the Cervical Lymph Glands.—This is most frequently seen in the secondary stage of syphilis when the mucous patches are present in the throat. The submaxillary glands may be as large as walnuts and moderately tender. Myriads of spirochetes are draining down from the mouth lesions to the lymph glands. It will be remembered that this is the dangerous stage of syphilis for the dentist. Primary chancre of the lip also causes similar enlargement of the regional lymph glands. Tertiary lesions originating within the lymph glands are quite rare. A gumma may occur in the overlying sternocleidomastoid muscle.

Lesions of the Musculature of the Face and Jaws.—**Trismus.**—A variety of pathological conditions lead to a prolonged spasm or contracture of the muscles in relation to the jaws so that the mouth can be opened with great difficulty if at all. This is known as trismus. It is more frequently due to a dental reflex than to any other cause. However, it is important for the dentist to know that there are other and general causes for trismus. The most important are the following:

Causes of Trismus.—

1. Dental reflexes—abscessed teeth, any acute inflammation in or about the teeth, impacted teeth, especially third molars may lead to a chronic spasm of the muscles of mastication. At times the source of the irritation is apparent only after prolonged search.

2. Lesions in the jaws:

- (a) Necrosis—as from phosphorus or mercury-poisoning or from chronic infection, such as tuberculosis or actinomycosis.
- (b) Osteomyelitis—from simple infection by local extension from teeth or by pyemic infection.
- (c) Periostitis—due to syphilis, typhoid or other infection or to trauma.
- (d) Fracture—this is usually obvious but at times when there is no displacement or when the history of trauma is lacking, as after a period of unconsciousness, after anesthesia or alcoholic intoxication, the question of fracture is not considered.
- (e) Tumors—periosteal sarcoma or other malignant growths invading the muscles attached to the jaws give rise to a certain amount of irritation.

3. Lesions of the Muscles:

- (a) Myositis or inflammation of the muscle tissue due to inflammatory rheumatism or other acute infection or to trauma.
- (b) Trichinosis or pork-poisoning in which the worm *trichina spiralis* penetrates the muscle fiber and sets up inflammatory swelling, tenderness and edema. In very acute cases there may be a marked degree of trismus. The toxin of this parasite causes a marked eosinophilia (increase in the number of eosinophilic leukocytes in the blood). This is an important diagnostic point.

4. Lesions of the Oral Cavity:

Painful forms of acute gingivitis, stomatitis, ulcer on the inside of the cheek and peritonsillar abscess may all induce considerable muscle spasm. In a highly neurotic individual, especially a child, a sharp throat infection may be associated with trismus.

5. Lesions of the Skin of the Face:

Acute eczema with the swelling and loss of elasticity of the skin may so interfere with the opening of the

mouth that dental work is impossible. This may be purely mechanical or there may be a degree of true trismus of the muscles associated with the inflammation of the skin. The same applies to any acute dermatitis or inflammation of the skin from burns or as a result of the action of irritant or poisonous substances.

6. Lesions in the Jaw Joint:

- (a) Arthritis, or inflammation of the joint, due to infection such as inflammatory rheumatism, gonococcus infection, arthritis deformans or other general infection. It may also be due to local extension from chronic middle-ear disease. Muscle spasm about inflamed joints is frequent anywhere in the body.
- (b) Synovitis and other irritative conditions due to trauma and recurrent dislocations of the jaw may cause mild trismus.

7. Lesions within the Skull:

- (a) Meningitis of any variety, meningococcal, tuberculous or septicemic. By irritation of the cranial nerves, especially the motor division of the fifth nerve, meningitis may cause trismus.
- (b) Brain tumor, especially in relation to Gasserian ganglion or fifth nerve. Pressure may be exerted here by marked increase of general intracranial pressure.
- (c) Apoplexy—cerebral hemorrhage. The patient is usually comatose and paralyzed. Occasionally the jaws are rigidly fixed.

8. General Disease:

- (a) Tetanus—of all extradental causes tetanus is the most important. Patients may be up as usual and come to the dentist's office with beginning trismus and the "Sardonic grin," due to tonic spasm of the facial muscles. The eyebrows are raised and the angles of the mouth drawn out. In cases in which the history of a wound is lacking, tetanus for a day or two at

least might easily be mistaken by the dentist for a reflex trismus. There would, of course, be some dental lesion in the patient. Tetanus at this stage may cause no fever. Acute cases with a short incubation progress rapidly to a fatal issue. Chronic cases coming on after a long incubation may clear up after a period of weeks. The trismus and sardonic grin gradually disappear.

Head Tetanus.—There is a form of head tetanus (Kopf-tetanus of Rose) arising from injuries of the head, especially in the distribution of the fifth nerve. With this there is trismus, but paralysis of the facial muscles on the affected side due to action of the tetanus toxin on the peripheral nerve fibers. There may also be difficulty in swallowing. The condition may remain local and run a chronic and favorable course.

- (b) *Hysteria*.—There is a hysterical or functional disorder of the nervous system associated with trismus. (The dentist, however, should guard against a hasty diagnosis of hysteria for such cases are frequently found to be due to organic disease.) Explosion is more likely to occur in a pathological nervous system than in a normal one. In fact, it is questionable if hysteria ever occurs in perfect health of the body in the sense in which health of the tissues was defined at the outset of the study of etiology. The chemical abnormalities of or intoxications that result from simple prolonged fatigue or from overeating or lack of elimination are definite departures from health. When marked they may cause more of a general poisoning of the body than local processes which are obviously due to organic disease. A hereditary instability of the nervous system in certain families and individuals, of course, causes

greater sensitiveness to minor departures from perfect health. In such individuals there may be no discernible cause for hysterical manifestations. Mental shock, fear or anxiety may be the indirect cause. Some of the unrecognized organic conditions with which hysteria may be confused or upon which genuine hysteria may be superimposed are cerebrospinal syphilis, meningitis, brain tumor, unsuspected fracture of the skull, hyperthyroidism, cardiovascular or cardiorenal disease, with high blood-pressure and chronic diseases, such as tuberculosis. Tetanus at onset has been mistaken for hysteria, especially when afebrile. Fever when present is a differential point in favor of tetanus. The subject of hysteria really involves all of the complexities of diagnosis and the dentist should remember that such patients usually want treatment and not contempt. Trismus associated with major hysteria is probably not due to a dental condition.

- (c) Tetany is a condition of nervous hypersensitiveness usually occurring in children and depending on some gastro-intestinal or other intoxication. There is a form of tetany occurring as an epidemic infection in certain parts of Europe. The same spasm of tetany may complicate many infectious diseases and also exogenous intoxications. It is characterized by bilateral spasmodic contracture (carpopedal spasm) in which there is inward rotation and flexion of the extremities. The thumbs are flexed into the palm and the forearm and foot rotated inward. There may be trismus and general muscular spasm or convulsions. Twitching of the facial muscles may be elicited by tapping over the exit of the facial nerve (Chvostek's sign). There may be similar spasm of the

laryngeal muscles, causing transient obstruction to breathing (laryngospasm, laryngismus stridulus). Many of these children are rachitic. Teething in them may cause trismus and fairly marked nervous symptoms. Usually, however, teething causes no more than moderate irritability and slight if any fever in healthy children. Tetany may occur in adults after goiter operations by accidental removal of the parathyroid glands. The parathyroids are closely related to the calcium metabolism of the body. Calcium salts taken by mouth are of value in the treatment of tetany generally. Accordingly it is considered probable that the parathyroid glands play a part in the etiology of tetany. In the so-called attack of the condition the muscular spasm may last hours or days and may recur with another exciting cause.

9. Lesions of the Parotid Glands:

Lesions of the parotid glands, especially of the part in close relation to the jaw, may cause trismus. This occurs in epidemic parotitis (or mumps) and in the secondary forms of acute parotitis, such as the parotitis complicating the bacteremic diseases and septicemia. Suppuration in this region may even burrow into the capsule of the jaw-joint or into the external auditory canal, causing an inflammatory fixation of all the movable parts. Malignant tumors of the parotid by pressure on or actual invasion into the same structures may produce a similar fixation of the jaws.

Atrophy of Muscles.—*Muscles of Mastication.*—Excision of the Gasserian ganglion or injury to the motor root of the fifth nerve is the cause of paralysis of the muscles of mastication. Being a unilateral lesion, usually there is little or no disturbance of mastication, but there may be difficulty in keeping food between the teeth on the affected side because of the paralysis of the buccinator and relaxation of the cheek.

There is, of course, atrophy of the muscles—most noticeable over the masseter and temporal muscles. There is atrophy of disuse in malformations of the jaws and in ankylosis of the jaw-joint.

Lesions of the Accessory Sinuses.—Simple Infections.—By direct extension along the mucous membrane from the nasal cavities any type of infectious or catarrhal inflammation may reach the maxillary antra, the frontal sinuses, the ethmoidal and sphenoidal sinuses and the middle ears and mastoid. This inflammation may accompany a common head cold or the nasopharyngitis of influenza, measles and other throat infections. Occasionally these sinus inflammations result in suppuration and abscess formation, especially if there is faulty drainage from the sinus. On account of the anatomy of the maxillary sinus with its flow lower than the drainage outlet, abscess or empyema is more frequent than in other sinuses as the frontal, where the drainage is downward from the most dependent portion of the cavity. Infection of the maxillary sinuses from the upper teeth is a much less frequent channel than from the nose. In doubtful cases there should be an exploratory puncture and irrigation of the antrum through the nose before sacrificing teeth. X-ray and transillumination are not always diagnostic.

Special Infections.—*Erysipelas* may extend inward from the nose or it may originate within the sinuses, especially the maxillary from an infected root of a tooth. The constitutional symptoms in such a case may be hard to explain until the advancing border of the eruption appears in the nose or mouth.

Diphtheria in the nasal form may extend so that the sinuses are lined with the characteristic membrane. This is, however, usually hopelessly late in the disease. Nasal diphtheria at best is a very virulent type of the infection and liable to be fatal unless treated very early with antitoxin.

Polyps.—Chronic inflammation and hyperplasia of the mucous membranes lead to thickening and to papillomatous growths, which histologically show the structure of fibromata or fibromyxomata. Polyps may be packed in the sinuses as densely as in the nasal cavities. They may be continuous

pressure cause marked pressure atrophy and bony deformity. In the frontal sinuses, polyps entirely benign and removable, may cause absorption of the thin inner bony wall of the sinus and greatly displace and compress the frontal lobes of the brain. Similar polypoid overgrowth may fill the maxillary sinuses and cause pain referred to the upper teeth, especially bicuspid and first molar. Granulation tissue after necrotic or ulcerative inflammation may similarly accumulate in the cavities of the sinuses.

Tumors.—*Epithelioma* occasionally arises in the mucous membrane of the sinuses especially the maxillary and may be first manifested by metastatic involvement in the regional lymph glands. Sooner or later there is direct invasion into and through the bony walls of the sinus.

Sarcoma may arise in the submucosa, periosteum or bone. These tumors may be of only moderate malignancy and at times reach great size, producing very unsightly deformity. The periosteal form is apt to be more malignant.

Teeth.—Anomalous eruption of teeth into the antrum occurs. Supernumerary teeth are also found. They may ultimately become carious and lead to abscess formation.

Lesions of the Cranial Nerves in Relation to the Oral Cavity.

—**The First Nerve.**—The olfactory nerve lesions are usually characterized by loss of smell (anosmia). This may be due to injury at the root of the nose, often together with fracture of the superior maxilla. It may also be due to degeneration in the peripheral fibrils from chronic rhinitis or nasal polyps. Intracranial disease may involve the olfactory bulbs with loss of smell. The normal nose, however, does not perceive the most foul breath exhaled through the nostrils.

The Second Nerve.—In the distribution of the second or optic nerve the main lesion that can be related to the teeth is retinitis, with hemorrhage and blindness in the affected area. Of late years many cases of retinal hemorrhage in young people have been attributed to focal and especially dental infections. The conclusion is arrived at more by the exclusion of other causes than by the presence of infected teeth. Optic nerve lesions are usually due to heart, artery or kidney disease or to syphilis and other constitutional conditions.

The Third Nerve.—The third or oculomotor nerve is the main motor nerve to the extrinsic eye muscles and to the iris. Lesions of the nerve cause squint (strabismus) and changes in the pupil. Like the second nerve, these lesions are practically always due to syphilis or general disease and never to a dental reflex. However, iritis like retinitis with hemorrhage may be due to metastatic infection from abscessed teeth. The pupil may be irregular and fail to react to light. A pupil, immobile to light but reacting with accommodation (Argyll-Robertson pupil) is characteristic of locomotor ataxia.

The Fourth Nerve (Trochlear).—This is unimportant supplying only the superior oblique muscle of the eye.

The Fifth Nerve.—The trigeminal or fifth cranial nerve is the most closely related physiologically and pathologically to the oral cavity. The fifth nerve is the sensory nerve to all the teeth and the motor nerve to the muscles of mastication. It also anastomoses with fibers of the seventh cranial or facial nerve, the motor nerve to the muscles of the face. Consequently lesions of the teeth may cause reflex irritations in considerable variety. The reflex arc may be by way of the Gasserian ganglion, so that *trigeminal neuralgia* may be referred to any or all of the three main divisions of the fifth nerve, the ophthalmic, the superior maxillary or the inferior maxillary. Pain may also be referred to another branch in the same division. For example, an abscessed tooth in the lower jaw may cause referred pain in the temple through the auriculotemporal branch of the inferior maxillary nerve.

Facial Tic, or involuntary twitching of the face, is occasionally due to an irritative lesion in the teeth. However, there are many forms that are independent of the teeth or any other focal lesion, and reflect a general neuropathic tendency or nervous instability.

The Sixth Nerve (Abducens).—Lesions cause paralysis of the external rectus muscle of the eye and internal squint. Etiological considerations are the same as in lesions of the third nerve.

The Seventh Nerve.—Facial paralysis resulting from a lesion of the facial nerve is a condition which the dentist

should not associate with diseases of the teeth. The lesion is either in the peripheral trunk of the facial nerve or it is intracranial. The peripheral nerve may be affected by disease in the middle ear or at the exit of the nerve from the stylomastoid foramen. This peripheral facial paralysis is known as Bell's palsy. The commonest intracranial cause is syphilis, although such other lesions as brain tumor and meningitis may cause facial paralysis.



FIG. 118.—Facial paralysis. (Brown.)

The Eighth Nerve.—The auditory and vestibular nerves are also quite independent of dental conditions so far as definite knowledge goes. Painful conditions in the region of the third molar tooth and tonsils cause a radiation of pain toward the ear, but deafness and vertigo result only from lesions of the middle and internal ear and semicircular canals or from intracranial or general disease. Possibly there is an occasional vertigo due to a vestibular neuritis of infectious origin such as oral sepsis.

The Ninth Nerve.—The glossopharyngeal nerve supplies motor fibers to the constrictor muscles of the pharynx and sensory taste fibers to the posterior part of the tongue. Loss of taste (ageusia) may result from lesions in this region.

The Tenth Nerve.—The pneumogastric or vagus (wandering) nerve is of interest to the dentist because it establishes a nervous connection between the oral cavity and the various viscera supplied by the vagus—mainly the lungs, heart, esophagus and stomach. Branches also supply the pharynx and larynx but not the teeth directly. Reflex disturbances of the several organs through the vagus are quite frequent. The irritative lesion may be intracranial at the nucleus of origin of the vagus or in the trunk or branches of the nerve. Any intracranial condition which increases intracranial pressure may cause vagus stimulation and the characteristic visceral symptoms such as slow heart action and respiration, vomiting and increased blood-pressure. This is seen in meningitis and in hemorrhage from fracture of the skull or in apoplexy. Pressure on the trunk of the vagus in the neck may cause similar effects. There may also be reflexes from one peripheral branch, which are referred to another branch. For example, a blow on the stomach inhibits respiration. The physiological facts are of interest in the interpretation of possible reflexes through the vagus. However, there is very little definite knowledge of vagus reflexes from lesions within the oral cavity proper. An infectious or toxic neuritis of the trunk of the vagus (vagus neuritis) occurs and the source of this may frequently be in the oral cavity—for example, diphtheria.

Bulbar Palsy.—There is a form of paralysis of the lips, tongue and larynx (glosso-labio-laryngeal palsy) due to atrophy of the nuclei of origin of the tenth, eleventh and twelfth cranial nerves. These nuclei lie close together in the floor of the fourth ventricle in the medulla or bulb. In bulbar palsy the tongue is seen atrophied and motionless in the floor of the mouth and the paralyzed lips do not prevent saliva from drooling constantly over them. This disease is one of a number of primary degenerations in the central nervous system (spastic paraplegia, etc.). Their etiology is unknown. Pathologically they are essentially simple atrophy when seen at autopsy. This is the end-stage of a long chronic process of disease. Of recent years some of these conditions have been brought into relation to dental

and other focal infections, just as iritis and certain forms of retinitis have been so related. It will be remembered that nerve cells are the most highly differentiated type of cell and have practically no power of regeneration. It is obvious that even if the whole disease were primarily due to metastatic infection from the teeth, extractions and complete eradication of focal infections would be of no avail after atrophy and sclerosis had occurred in the central nervous system. A progressive process, however, might be arrested. If this etiological relation could be definitely established it would lead to a much more radical treatment of dead teeth. The dentist should remember again that the relation of dental infection to lesions in the central nervous system must be considered only after the exclusion of the usual etiologic agents in nervous disease. Chief among these is syphilis, but any chronic infection or intoxication may lead to these degenerations in nervous tissue.

The Eleventh Nerve.—The spinal accessory nerve supplies mainly the sternocleidomastoid and trapezius muscles. Tumors and abscesses of the neck, and especially large masses of tuberculous lymph glands, may press on the eleventh nerve. The nerve may be cut in operations for the removal of these glands. The result is paralysis and atrophy of the muscles supplied. The most noticeable effect is the "shoulder drop" on the affected side due to paralysis of the trapezius.

Torticollis (wry-neck).—Spasmodic contractions, either tonic or clonic, result from involvement of the sternocleidomastoid and allied muscles. Spasmodic torticollis is comparable to facial tic. The head is jerked intermittently to the side, the chin turning toward the sound shoulder and slightly upward. The condition is especially liable to occur in neurotic individuals, as in the case of facial tic, and no other cause may be found. However, any reflex from a focal irritation should be eliminated. Abscessed teeth should be removed but the dentist should not be too sanguine in regard to cure or even improvement of torticollis.

The Twelfth Nerve.—The hypoglossal nerve is the motor supply to the muscles of the tongue. Paralysis leads to

atrophy of the tongue as described under bulbar palsy. Spasm of the tongue is rare, but cases have been described which seemed to follow reflex irritation of the fifth nerve, especially from the teeth.

In conclusion, it is hoped that this review of the lesions of the oral cavity and allied structures will impress the dentist that the mouth is really very closely related to the general pathological processes and systemic infections.

CHAPTER XVII.

FOCAL INFECTION AND DISEASE RELATED TO FOCAL INFECTION.

THE subject of focal infection is one of the new and growing fields of medical research and at the same time constitutes the main borderland between dental and general medical diagnosis. Although focal infection has been suggested as an etiologic agent for a long time it is only in the last ten or fifteen years that the subject has been developed in a scientific and practical way. There is still a great amount of conflicting evidence on the etiological relation of focal infection to certain systemic diseases. There is at present a great deal of unwarranted enthusiasm on the one extreme and a great deal of indiscriminating nihilism on the other. The problem is a very complex one on account of the multiplicity of primary foci of infection and of the uncertainty of secondary foci and also on account of the great variety in the kinds and virulence of the infecting organisms and in the local and general resistance of the host. In a given case there may be an extraordinary amount of infection as in a badly neglected mouth with multiple root abscesses and extensive pyorrhea and yet without any signs of systemic absorption. On the other hand there may be an acute or chronic septicemia from a focus so insignificant that it would seem almost incredible that it could be the entire source of the generalized infection. Exactly this occurred in a case seen by the author. The patient died of a hemolytic streptococcus septicemia. A complete autopsy showed absolutely nothing but the same infection in a localized abscess which originated in the upper second bicuspid and first molar teeth and extended to the maxilla. In this case also there was evidence in the form of a gradually increasing anemia for many months,

of a slow or intermittent escape of the hemolytic organisms into the blood stream without any signs of local inflammation or pain. Finally local edema and tenderness did develop as in the ordinary acute tooth abscess. Extraction was then done and the septicemia resulted and proved fatal about six weeks later.

APPARENT INCONSISTENCIES IN THE EFFECTS OF FOCAL INFECTION.

All infectious diseases show in individual cases, great variations which really represent the resultant of the above-mentioned factors. In pneumonia it is a frequent observation to see an intense toxemia with a very small amount of infiltration of lung. By contrast pneumonia with a massive consolidation of a large part of both lungs may cause a comparatively mild toxemia. A boil may result in septicemia, while an enormous abscess may heal without any complication. A mild tonsillitis may cause a nephritis or an endocarditis; a severe infection of tonsils, peritonsillar and glandular tissues may be uncomplicated. Chronic infections show an even wider range in their clinical course. Tuberculosis for example is not always curable when recognized in incipient form. On the other hand advanced cases not infrequently live to a good old age. Seventy-five per cent. or more of people have had the seed of tuberculosis sown in their tissues but only in about 1 per cent. does it ever become more than a local or focal infection. If 99 per cent. of focal infections about the teeth caused no symptoms, we would still have widespread morbidity from the remaining 1 per cent. because of the great frequency of infected teeth. It means nothing therefore that large numbers of healthy people, soldiers for example, as shown by routine x-ray examinations of the teeth, have numerous large abscesses without symptoms. Health implies good general resistance and large dense abscess walls imply good local resistance; both imply relatively low virulence in the infecting organism.

**FURTHER EVIDENCES OF THE ETIOLOGICAL RELATION
BETWEEN FOCAL INFECTION AND SYSTEMIC
DISEASE.**

Evidence must be obtained in different ways in different diseases. In some unfortunately the only way is that of establishing the probability of the focal infective origin as based on a large number of observations in the same disease. Some more positive evidences may be stated as follows:

1. *Identity of Organisms in the Infective Foci to Those Obtained from the Lesions of the Disease.*—This can be established only in the specific organisms such as the tubercle bacillus or the typhoid bacillus. The various types of streptococci and pneumococci have a certain degree of specificity. Advances in the bacteriology of the pyogenic cocci may yield very important evidence in connection with focal infection. Elective localization in certain tissues by special strains of streptococci is the newest phase of the subject but will bear further confirmation.

2. *Establishment of a Time Relation Between the Development of Infective Foci and the Appearance of Systemic Symptoms.*—For example tonsillitis or a tooth abscess followed by a joint inflammation.

3. *Establishment of a Time Relation Between the Appearance of Symptoms and a Lowering of General or Local Resistance Resulting in an Extension or Generalization of Infection.*—For example exposure to cold followed by acute streptococcal nephritis in a patient with chronic streptococcus infection at the roots of dead teeth. Chronic arthritis deformans may develop *pari passu* with the advances of age and lowering resistance as a result of arteriosclerosis.

4. *Prompt Relief in the More Acute Conditions Upon the Eradication of the Infective Foci.*—For example relief from acute neuritic pain after the extraction of an abscessed tooth.

5. *Demonstration of Persistent Secondary Foci of Infection Explaining Symptoms in Chronic Infective Diseases Unrelieved by Eradication of Primary Foci.*—For example arthritis deformans showing extensive infection in the joints at

autopsy long after removal of all primary foci. Secondary foci may be widespread and quite inaccessible.

6. *Similarity of Lesions of a Disease to the Lesions of Known Infections.*—For example again the early lesions of arthritis deformans are practically identical with those of an infectious arthritis. Gout by contrast is quite a different process pathologically.

7. *From the Dental Standpoint the Age Incidence of a Disease in Relation to the Age Incidence of Dental Caries, namely, Greatest in the Third Decade.*—Some statistics show as high as 40 per cent. of cases of arthritis deformans beginning before the age of thirty years.

ORGANISMS IN FOCI OF INFECTION AND THEIR LOCATIONS.

The most important organisms found in the focal infections are the pyogenic cocci. The various types of streptococci, *S. hemolyticus*, *S. viridans* and *S. mucosus* are more apt to be virulent and invasive. They are the common organisms about the teeth and tonsils. The *staphylococci* are also frequently found. *Pneumococci* in any of the four types that may be serologically differentiated frequently occur in foci in the accessory sinuses of the nose, in discharging ears and in the lungs. The *meningococcus* occurs in the naso-pharynx of convalescents and carriers of epidemic meningitis. The *gonococcus* is frequent in the prostate and seminal vesicles and in the Fallopian tubes. The *colon bacillus*, the *typhoid bacillus* and cocci may be found either associated or separately in the gall-bladder or less frequently in ulcers and fistulæ in the gastro-intestinal and urinary tracts. There are sometimes persistent miliary abscesses in the kidney following typhoid fever. Colon bacillus infections of the urinary tract (cystitis, pyelitis) are frequent. The appendix may harbor a chronic infection. Sinuses about the rectum, from bone abscesses, from tuberculosis of lymph glands, from infections around foreign bodies and suppurative processes of great variety are all focal infections. In these any pathogenic organisms may be found. As a matter of fact,

however, the clinical evidence in reference to focal infections indicates strongly that the most important organisms are the pyogenic cocci and the most frequent locations of primary foci are the teeth, tonsils and accessory sinuses. Many of the other infected areas really represent secondary foci.

DISEASES RELATED TO FOCAL INFECTION.

Osseous System.—The joints are among the most vulnerable structures in relation to focal infection. This may be due partly to their low vascularity and in some cases to the local trauma from use. The analogy to pyemic joint infections is suggestive and also the frequency of arthritic complications in the bacteremic diseases. Acute joint infections, such as inflammatory rheumatism, are usually associated with tonsillar infection; while chronic infections, especially arthritis deformans, apparently originate more frequently in dental infections as the primary foci.

Acute Inflammatory Rheumatism.—Long before the days of bacteriology it was clinically recognized that acute rheumatism frequently followed directly after an attack of tonsillitis. At times the joint inflammations appear at the height of the tonsillitis which may then continue in subacute form for weeks. All the features of inflammatory rheumatism are characteristic of an infectious process. Fever, leukocytosis, sweating, secondary anemia and albuminuria are practically constant accompaniments of the disease and endocarditis is a more frequent complication than with any other infection. Typically, acute rheumatism runs a self-limited course of about six weeks. However, there are subacute and chronic forms which may last for months. Some of these cases promptly clear up after removal of tonsils and a low-grade fever curve may drop at once to the normal level. There is no agreement on any specific organism as the cause of rheumatism, although the *micrococcus rheumaticus* has been described. Some observers believe the infection to be due to a variety of streptococci. As in other streptococcus infections, a scarlatiniform eruption is occasionally seen.

There is usually successive involvement of a number of joints, most commonly of the knees and ankles. Marked hyperemia of the synovial membranes and of the periarticular structures occurs. There may be a small amount of turbid joint fluid but never copious effusion nor suppuration. The great frequency of endocarditis is also confirmatory of the etiology of rheumatism as a blood-borne infection. The mitral valve is usually the first attacked. A chronic infection may persist here for an almost indefinite period and become more established with each subsequent attack. The heart valves then become secondary foci of infection. Unfortunately this is frequently the case in valvular heart disease, so that removal of the primary focus does not modify the course of the disease. The infection in a mild endocarditis, however, if there are not recurrent attacks may entirely die out. The scar tissue remaining may represent an area of localized lowered resistance, so that it may be infected more easily than in the first attack. Subsequent attacks may come from a variety of focal infections after the original focus is removed. It is in this connection that dental infection finds its most important relation to heart disease. Even in the degenerative heart diseases in the second half of life, an infectious process may be superimposed by the constant filtering of organisms into the blood-stream from infected foci. The final heart failure is often due to a fresh endo- or myocarditis. Occasionally, however, a primary endocarditis may result from an acute tooth abscess.

Chorea.—Chorea or *St. Vitus's Dance* is a manifestation of the rheumatic infection involving the nervous system. Organisms can be demonstrated in the cortex of the brain. Endocarditis occurs just as in joint rheumatism. Focal infections, especially in the tonsils, are closely related to chorea, although a neuropathic heredity and excessive nervous stimulation are at least predisposing factors. It is most common in childhood (especially in girls) but may recur later in life at times when the general resistance is reduced. Pregnancy is a recognized cause of such a recurrence. Again, focal infections may supply the direct exciting cause.

Arthritis Deformans.—This includes a wide variety of clinical forms of joint infections. Usually there is a slow insidious onset and a progressive course ending in permanent deformities of the joints. Any of the focal infections may be the cause, but the teeth are more implicated in these chronic cases than in acute rheumatism. A few cases, however, begin in the form of an acute polyarthritis indistinguishable from inflammatory rheumatism. The majority of cases begin during the second and third decades. Not a small group will develop years after all the teeth are lost. Some of the causative infections in these cases may be persistent secondary foci which originated in the oral cavity. Residual foci within the edentulous jaws have been demonstrated. There is also a rare type in children before the second dentition, known as Still's disease. Intestinal infections may be the primary source in these cases. The small joints of the hands are usually attacked first, producing a characteristic deflection of the fingers to the ulnar side and atrophy of the interosseous muscles. The larger joints show extensive hyperostosis and ankylosis. The spine may be involved alone, as in spondylitis deformans.

Predisposing causes undoubtedly play an important part in arthritis deformans. Hereditary factors are apparent in certain families. The so-called arthritic diathesis may depend on definite metabolic disorders. Such predisposing conditions, however, are not evidence against the direct infective etiology. On the contrary they make prophylaxis against focal infection more imperative. In all cases, after infection is thoroughly established in the joints, treatment is practically useless so far as radical cure is concerned. The prophylaxis of chronic arthritis then is the opportunity of the dentist in his management of infected teeth and pyorrhea. The *x*-ray will not show all dental infection. If a disabling or progressive arthritis is threatening it is justifiable, after excluding other foci of infection, to sacrifice all dead teeth, even with negative *x*-ray findings. This does not imply a radical position in reference to dead teeth generally in the absence of signs of systemic absorption.

Differential Diagnosis.—The dentist should keep in mind that there are other diseases of the joints which must be differentiated from arthritis deformans. The common ones with the important diagnostic points are the following:

Chronic Gout.—Type of patient; tophi; x-ray findings; uric acid metabolism.

Tuberculosis.—Usually monarticular; tuberculosis in lungs or elsewhere. Fever, muscle spasm; cold abscesses; x-ray findings.

Gonorrheal Rheumatism.—History of gonorrhea. Usually a self limited course. With secondary infection may become a form of arthritis deformans.

Syphilis of Joints.—*Secondary*; subacute and self-limited. *Tertiary*; chronic with predilection for the spine, simulating the spondylitic form of arthritis deformans. X-ray; syphilis elsewhere; Wassermann reaction.

Tabetic Arthropathy or Charcot Joint.—Painlessness, hypermobility; fixed pupils and lost knee-jerks of locomotor ataxia. Wassermann reaction.

Sarcoma of Joint.—One joint involved, steady growth, signs of malignancy; x-ray findings.

Traumatic Arthritis.—History of trauma; foreign body; x-ray.

Osteomyelitis.—This is another form of pyogenic infection in the osseous system. The bone marrow especially near the epiphyseal line in the ends of long bones in children provides good soil for the lodging and growth of organisms carried in the blood-stream from foci of infection. In the mandible it may be a direct extension from a root abscess. Osteomyelitis is most commonly a staphylococcus infection. Again predisposing factors are important, such as malnutrition, anemia, tuberculosis, gastro-enteritis and the convalescent state after acute diseases, such as typhoid fever, in which case the typhoid bacillus may be present. The abundant staphylococcus infection in skin lesions such as furunculosis and impetigo is an important source of osteomyelitis as well as teeth, tonsils and other foci. Acute osteomyelitis, when promptly drained, heals favorably. Chronic forms lead to extensive destruction of the shaft of the bone and discharging

sinuses that may never heal. Such conditions therefore represent very firmly established secondary foci of infection.

Periostitis.—Primary periostitis is less suggestive of focal infection than the above lesions of the osseous system. Of course there may be a direct extension from a dento-alveolar abscess to the periosteum of the mandible. Parulis is such a localized periostitis. It may also be secondary to osteomyelitis. The common causes of primary periostitis, however, are trauma and syphilis. The shin is a frequent site of both. The radiograph of syphilitic periostitis is very characteristic, showing a diffuse thickening with a wavy outline. Pyogenic infection carried from distant foci may be implanted secondarily especially in acute traumatic periostitis.

Fibrositis.—This is a term applied to localized inflammatory infiltrations and fibrous thickenings around bones and in the subcutaneous tissues and muscles. Painful nodules appear in the lumbar region of the back, between the scapulæ and over the supraspinatus and trapezius muscles. The condition has been included in the loosely termed "muscular rheumatism" which is no definite pathological entity. Focal infection probably is responsible for some of the cases of fibrositis, but doubtless many such lesions result from trauma, exposure and chronic intoxications.

Circulatory System.—Heart.—Most heart disease results from infection carried in the blood-stream. There are toxic and senile degenerations independent of infection especially in the second half of life, but even in these a secondary infectious process is frequently superimposed. The valvular heart disease of young people is in about 80 per cent. of cases the result of inflammatory rheumatism. As stated the tonsil is the most common atrium of infection. Tooth infections, localized abscesses, carbuncles, suppurative wounds and all of the infectious diseases occasionally set up an endocarditis, less frequently a myocarditis or pericarditis. The general nature of heart disease and its relation to dentistry have already been discussed. It remains only in connection with the subject of focal infection to emphasize the fact that the most important practical consideration is that of preventing infection or reinfection. Whatever organic

damage is done in the cardiac valves or musculature is irreparable. In the milder defects the heart compensates perfectly and the circulation may be carried on normally for an indefinite period, so long as a fresh infection is not set up. When the final breakdown does come, even though apparently due to overstrain, autopsy frequently shows that a fresh endocarditis had been present as the direct cause. Overstrain, of course, by quickening the heart rate and increasing local trauma on the valves, as well as by reducing the general resistance, predisposes strongly to infection of the endocardium by any organisms that may find their way into the blood-stream. In elderly people, therefore, and in chronic heart cases, it is important to enjoin complete rest during the entire course of an acute infectious process, such as an abscess in the oral cavity or neck.

Vascular System.—Many of the same considerations apply to the bloodvessels as to the heart with reference to infections. The *veins* are the most frequently involved. Inflammation and thrombosis result (thrombophlebitis). The femoral veins especially the left and the intracranial venous sinuses are common sites. The great majority of cases of phlebitis have a very obvious cause in the form of a bacteremic disease such as typhoid fever or a regional infection such as a mastoid abscess adjacent to the lateral sinus. It is in connection with the occasional unexplainable cases of phlebitis, that the matter of obscure focal infection comes up. There are cases of multiple and recurrent inflammations in the peripheral veins (phlebitis migrans). Erythema nodosum is a terminal phlebitis of this sort usually in rheumatic patients. Sometimes cocci can be grown from the blood-stream. Tonsillar and tooth infections are important sources to be considered.

The arteries are less easily infected. Endarteritis may be infectious or non-infectious. There may be a localized proliferation of the intima to the point of obliterating the lumen of the vessel. The dentist should know that in the primary etiology of arteriosclerosis, focal infection plays a very small part. Arteriosclerosis is a slow degeneration resulting from the greatest variety of intoxications, infections

and from the simple wear and tear of time. A curious feature of sclerosis of the smaller vessels, especially when associated with high blood-pressure is an increased irritability of the vasomotor nerves. Vasomotor spasms or so-called *vascular crises* occur in which there is a transient or intermittent closing of the vessels, with a corresponding loss of function of the affected part. If this is the motor cortex of the brain, there is a temporary paralysis or aphasia. A variety of exciting causes may induce vascular crises such as digestive disturbances, intoxications and infections. Focal infection especially about the teeth in elderly people is an exciting factor in some of these cases.

In the smaller vessels a localized infection may cause a small hemorrhage. A petechial skin eruption is very characteristic of sepsis. Hemorrhage into the retina is frequent. A milder local reaction in the smaller vessels and capillaries may lead to a localized vasomotor paralysis as in the rose spots of typhoid fever. Some cases of chronic urticaria or hives have been reported to have cleared up promptly after teeth extractions. Anaphylaxis may play a part in these vasomotor disturbances.

Blood Diseases.—Anemia.—Secondary anemia undoubtedly may result from focal infection and in the case of hemolytic streptococcus infection about the teeth an anemia of high grade may be produced. However, because of the extraordinary diversity of causes of anemia only a very small proportion of cases are really due to the ordinary focal infections. The more common causes of secondary anemia may be divided into four groups as follows:

Hemorrhage.—Wounds; ulcers—especially gastric; menorrhagia—fibroids; hemorrhoids; hemoptysis—thoracic diseases; hematuria—stone in the kidney.

Infectious and Parasitic Diseases.—Tuberculosis—syphilis—malaria—rheumatic and other fevers; intestinal parasites—hookworm, fish tapeworm.

Intoxications.—Metals and industrial poisons—lead, arsenic; food poisonings—gastro-intestinal stasis.

Malignant Tumors.—Cancer, sarcoma.

The dentist should understand that the interpretation of so

general a symptom as anemia is quite outside the dental field. It is only after the exclusion of the common systemic causes that anemia can be brought into relation to the teeth. Attempts to correlate minor variations in the blood count with dental conditions as described in recent literature are absurd unless very careful and complete general examination is carried out at the same time.

Pernicious Anemia.—The nature of the disease has been previously discussed. The relation to focal infection is uncertain. The removal of such foci does not cure the disease at least after the typical picture of pernicious anemia is established. A possible earlier stage or a milder anemia that clears up after the removal of any cause is at once regarded as a secondary anemia. Nothing is known of the causes, infectious or toxic, that may be operative on the blood-forming organs for long periods before actual pernicious anemia develops. It would be impossible to disprove that focal infection plays a part in this way. Some patients will give the history of mild anemia for many years before the onset of the pernicious symptoms. In a recent case in a woman who died at the age of fifty after a typical series of remissions over a period of four years, there was considerable anemia at the age of twenty years. She had extensive dental infection at that time and carried about sixteen dead teeth for many years. Under the crowns there was extreme resorption of the roots. This of course is only suggestive, but it is quite probable that some prolonged toxic or infectious action antedates the clinical course of pernicious anemia. In the aplastic form of the disease there is a complete failure of the function of hemogenesis. Similar presumptive evidence may be adduced in connection with the etiology of a number of the so-called idiopathic diseases, such as certain primary degenerations in the central nervous system. From the dental standpoint therefore, prophylaxis is important until the subject is more fully understood.

Leukemia.—There are two main theories of the etiology of this primary blood disease—one that it is a neoplastic process, the other that it is an infectious process. The first must remain rather meaningless until the etiology of tumors is

known. In support of the infectious theory, there is considerable clinical and some bacteriological evidence. There have been some observations on preleukemic conditions of the blood suggesting that the fatal disease as known clinically represents the final breakdown of the physiological reaction to chronic infection. In this way focal infection is implicated. The disease may be a manifestation of chronic sepsis. No specific organism is known.

Digestive System.—Most of the diseases of this system are independent of focal infection. Some of course will be complicated with secondary infection which abounds in the gastro-intestinal tract. Much of the bacterial life of the gastro-intestinal contents is saprophytic to the local tissues. Pathogenic organisms may be introduced constantly from infectious processes in the mouth and it is also possible for the same organisms to arrive at the same destination through the blood-stream.

Gastric and Duodenal Ulcer.—The exact etiology is not known. There may be different causes in different cases. Anything which overcomes the normal resistance of a part of the stomach wall allows that part to be acted upon by the digestive ferments. Local absence of the normal antiferment may be an immediate cause. This may depend upon a local circulatory disturbance—a local anemia or infarction. It may follow a prolonged chronic catarrhal inflammation such as that associated with alcoholism. In some cases it seems to be a local manifestation of a general toxemia as in the case of duodenal ulcers following large superficial burns. Finally focal infection seems to be implicated in a certain proportion of cases. In all cases it is certain that it is undesirable to have irritant and infectious material from the mouth as in bad pyorrhea pouring into an ulcerated stomach. In some cases it is probable that focal infections in teeth and tonsils bear a direct etiological relation to gastric ulcer. In these cases infectious foci should be eradicated thoroughly for ulcer has a tendency to recur, even after apparently healed.

Gall-bladder Disease.—*Cholecystitis*, *Cholelithiasis*.—Infection is the cause of gall-bladder disease. Bacteria may

come from the alimentary tract through the ducts, through the portal circulation or from distant foci of infection through the general circulation. All conditions favoring stasis in the biliary tract predispose to infection. There may or may not be concretions or gall-stones. Organisms are frequently found at the center of recent gall-stones. Streptococci and other pyogenic cocci are frequent. Colon bacilli and typhoid bacilli are also found. The hematogenous route of infection of the gall-bladder is probably the usual one. The bile represents a channel of excretion. Stagnation in the gall-bladder therefore affords favorable conditions for the accumulation of organisms from the various foci of infection. Cholecystitis may result in suppuration and peritonitis.

Dental Considerations.—Again from the dental standpoint, prophylaxis is important. Crowned teeth with abscessed roots may be left for years with apparent impunity. The occasional organism that escapes into the circulation seems to cause no trouble. Later gall-stone colic may suddenly come on, apparently without cause. The stone, however, represents a late stage of an old infectious process. With a secondary focus of infection thoroughly established in the gall-bladder, removal of the primary focus is futile so far as any curative effect is concerned.

Appendicitis.—This common disease is also an infection. The appendix is a retrogressive structure and is composed largely of lymphoid tissue, the same as the tonsil. The anatomy of the appendix, as a narrow, blind tube also predisposes to infection. Fecal concretions and foreign bodies are often present. Presumably the organisms nearest at hand are usually responsible. However the streptococcus is a very frequent offender and many believe that hematogenous infection frequently occurs. In septicemia, appendicitis is sometimes among the local manifestations of the general infection. However, the relation of appendicitis to focal infection is less definite than of gall-bladder disease to focal infection. Influenzal appendicitis sometimes occurs.

Genito-urinary System.—The kidney represents the main channel of excretion from the blood. Foreign substances and organisms as well as normal constituents are con-

centrated in their elimination through the kidney filter into the urine. Foreign substance such as the dye, phenol-sulphone-phthalein injected into any part of the body, appears in the urine in a very few minutes and 70 per cent of it is excreted in two hours. The occasional organism finding its way into the blood-stream from focal infections is usually either destroyed or excreted into the urine. Urine obtained by ureteral catheter, although normally sterile in ordinary health, not infrequently shows a few colonies on culture.

Nephritis.—From the above considerations it is readily understood why nephritis is a common complication of the acute infectious diseases. Toxic injury of the kidney may be the entire cause of nephritis or may pave the way for actual infection. Exposure to cold has long been known to predispose strongly to nephritis. Originally it was believed to be the entire cause, but in many of these cases, streptococci can be demonstrated in the urine and in the kidney. Their origin is hematogenous from chronic foci of infection. Chronic nephritis may follow acute nephritis. There is a form of chronic interstitial nephritis, however, (the ordinary Bright's disease), which comes on insidiously as a slow degenerative process like arteriosclerosis. This has a complex etiology, in which focal infection is at most one of many contributing factors.

Pyelitis.—This is an inflammation of the pelvis of the kidney. Its relation to focal infection is much the same as that of nephritis. It is more exclusively an infectious process, and the colon bacillus plays a larger part in its etiology than in nephritis. Lymphatic connections with the adjacent bowel may be responsible for some of these cases. Obstruction to urinary outflow such as pressure of the pregnant uterus upon the ureters or hypertrophy of the prostate is an important predisposing cause. Pyogenic cocci of focal infective origin may be present. There may be an associated involvement of the kidney (pyelonephritis). There may also be concretions or stones (nephrolithiasis), or finally extensive suppuration (pyonephrosis).

Tuberculosis of the kidney or urinary tract is secondary

to tuberculosis elsewhere. It may be a small focus in the lung or in a lymph gland. The organism is carried in the blood-stream just as in any pyogenic focus of infection. In fact there frequently is secondary pyogenic infection in renal tuberculosis, just as in a tuberculous lymph gland of the neck.

Prostatitis and Seminal Vesiculitis.—This is usually gonorrheal in origin. It is frequently secondarily infected and becomes a very obstinate focus of infection. Hypertrophy of the prostate in old men readily leads to local infection. Also tuberculosis of these parts favors a pyogenic invasion. Consequently this region is one of the important extra-oral foci to be kept in mind in the practical management of patients.

Respiratory System.—This system is related to the subject of focal infection mainly as a region of possibilities in the way of obscure foci. Tuberculous ulcers and cavities harbor secondary infection, pneumococcus, staphylococcus and streptococcus among other types. Chronic bronchitis especially with localized dilatations (bronchiectasis) presents similar conditions. Persistent influenzal infection abounds since the great pandemic.

Asthma.—Asthma is a spasmodic contraction of the muscular wall of the bronchioles (bronchiolar hypertonus). Its etiology is complex and poorly understood. Anaphylactic sensitization to certain substances is one factor. The substance may be bacterial protein or toxin from foci of infection either in the bronchial tree or elsewhere, such as teeth and tonsils. The irritation of such lesions may also act through a nervous reflex causing a constriction of the bronchioles. These pulmonary and bronchial foci must be treated mainly by the slow method of raising the general resistance by tonic and hygienic measures and by autogenous vaccines. The latter are of rather uncertain efficacy in their present stage of development.

Nervous System.—The nervous system is subject to primary infections and is involved in a great variety of general diseases and intoxications. Syphilis is a prolific cause of disease of the central nervous system. Hereditary and

familial factors play a larger part in the etiology of nervous disorders than in disease of the less highly specialized organs. Focal infection comes up after the exclusion of these major causes or as a contributory cause in nervous disease.

Neuralgia and Neuritis.—Nerve irritation may result from any of the above causes. It is very frequent during and after infectious diseases such as influenza, diphtheria and typhoid, with such intoxications as alcohol and lead and with metabolic toxemias such as diabetes. In a considerable group of cases, however, no such cause can be made out and it is in these cases that the search for foci of infection becomes important. The nerves to the extremities, the brachial and sciatic are especially susceptible. The sciatic nerve roots in addition to the above factors may be injured mechanically by the pressure of tumors in the pelvis or at the intervertebral foramina by arthritic excrescences. The latter are frequently due to focal infection. When an abscessed tooth is sealed shut with a treatment and left several days neuralgic pains are often produced in distant parts, such as in the brachial distribution. Relief may be prompt upon opening the tooth. This is really an experimental demonstration of the mechanism of neuritis of focal infective origin.

The cranial nerves have already been separately considered. Other peripheral nerves are similarly involved.

The Primary or Idiopathic Degenerations of the Brain and Spinal Cord.—These have also been considered and their possible relation to focal infection pointed out. Even if there is a predisposing cause in heredity in many cases, there may be, as in arthritis deformans, a very definite exciting cause which is much more amenable to treatment. Here again prophylaxis is of prime importance. These diseases have a variety of names, most of which simply designate the location of the lesion, such as postero-lateral sclerosis, or describe the symptom complex, as spastic paraplegia. Nothing definite is known about their etiology. Pathologically they show a non-specific degeneration. Of recent years, considerable evidence has been accumulated to indicate the causal relation of focal infections. The future will undoubtedly add further data.

Functional Nervous Disorders.—Here again all the causes of nervous disease may be at work and in addition all conditions of fatigue, worry, perverted habit and poor hygiene. No cases require more exhaustive study than the so-called neurasthenics. Unrecognized organic disease is frequently the underlying cause. Chorea for example has been regarded as a functional nervous disease, but now is considered almost universally to be due to a form of rheumatic infection. A pathological nervous system is more apt to have functional disturbances such as hysteria than the normal nervous system. Focal infection is simply one of the many factors involved and is to be arrived at largely by exclusion. Some forms of *insanity* show no demonstrable pathological changes. Hereditary nervous instability is usually present. However, in the most progressive institutions for the insane, an exhaustive search for focal infections and irritations is made and radical treatment carried out. The resident dentist is a regular member of the staff. The nose, ear and throat specialist also has an important field in this connection. Good authorities believe that definite results are obtained in certain cases.

Special Senses.—With the exception of the eye the nerves of special sense have been sufficiently considered under the cranial nerves. Many structures in the eye are subject to diseases of focal infective origin. Competent ophthalmologists have written extensively on iritis, retinitis, choroiditis and other conditions with this etiology. *Iritis* may be taken as an example. It has a complex etiology. It is very frequent in syphilis either in the secondary or tertiary stage. A number of the systemic diseases may be the underlying cause. In pyemia, there may be any type of eye involvement even sloughing of the whole eyeball (panophthalmitis). There are a great many cases of iritis, however, in which absolutely no systemic cause can be found, except foci of infection. Prompt cure after the removal of such foci in some of these cases has been very striking. On account of the seriousness of persistent eye lesions "doubtful" teeth should be sacrificed. On the other hand, in disturbances of vision with a possibility of brain tumor, it is very important not to

lose valuable time in the treatment of focal infections. Choked disk or swelling of the head of the optic nerve means an increase in intracranial pressure not focal infection. If the pressure is not relieved early, there may be permanent disturbance of vision or even complete blindness.

In conclusion, it is hoped that the dentist may gain from the above résumé a broader conception of the possibilities of focal infection and of the relation of dentistry in general to medicine. The large proportion of diseases of obscure etiology in the list indicates that much yet remains to be done. The scientific dentist can contribute valuable data to the solution of some of these problems especially by intelligent coöperation with medical men.

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